HARAMAYA UNIVERSITY

SCHOOL OF POST-GRADUATE PROGRAM DIRECTORATE

PREDICTORS OF SURVIVAL TIMEAMONG CHILDREN ON ANTIRETROVIRAL THERAPY IN DILCHORA REFERRAL HOSPITAL, DIRE DAWA, EAST ETHIOPIA

MPH Thesis

Addisu Belachew

December, 2019

Haramaya University, Harar

PREDICTORS OF SURVIVAL TIME AMONG CHILDREN ON ANTIRETROVIRAL THERAPY IN DILCHORA REFERRAL HOSPITAL, DIRE DAWA, EAST ETHIOPIA

A Thesis Submitted to the School of Public Health,School of Graduate Studies, Haramaya University in Partial Fulfillment of the Requirement for the Degree of Master in Public Health Nutrition

Addisu Belachew

Major advisor: Tariku Dingeta (MPH, PhD Candidate)

Co-advisor: Melake Demena (MPH, Assistant professor)

December, 2019

Haramaya University, Harar

APPROVAL SHEET

HARAMAYA UNIVERSITY

SCHOOL OF GRADUATE STUDIES

I hereby certify that I have read and evaluated this Thesis entitled "predictors of survival time among children on antiretroviral therapy in Dilchora referral hospital, Dire DawaEast Ethiopia. I recommend that it be submitted as fulfilling the thesis requirement.

Tariku Dingeta (PhD Candidate)_____

Major Advisor Signature Date

Melake Demena (MPH, Assistant professor)_____

Co-Advisor Signature Date

As a member of the Board of Examiners of the MPH Thesis Open Defense Examination, I certify that I have read and evaluated the Thesis prepared by Addisu Belachew and examined the candidate. I recommend that the Thesis be accepted as fulfilling the Thesis requirements for the degree of Master of Public Health in Public Health Nutrition.

_____ _____ _____

Chair Person Signature Date

_____ _____ _____

Internal Examiner Signature Date

_____ _____ _____

External Examiner Signature Date

Final approval and acceptance of the Thesis is contingent upon the submission of its final copy to the Council of Graduate Studies (CGS) through the Candidate's Department or School Graduate Committee (DGC or SGC).

STATEMENTS OF THE AUTHOR

By my signature below, I declare and affirm that this Thesis is my own work. I have followed all ethical and technical principles of scholarship 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.

This Thesis is submitted in partial fulfillment of the requirements for Master of Public Health degree at Haramaya University. The Thesis is deposited in Haramaya University Library and is made available to borrowers under the rules of the Library. I solemnly declare that this Thesis has not been submitted to any other institution anywhere for the award of any academic degree, diploma or certificate.

Brief quotation from this Thesis may be made without special permission provided that accurate and complete acknowledgement of the source is made. Requests for permission for extended quotations from or reproduction of this thesis in whole or in part may be granted by the Head of the School or Department when in his or her judgment the proposed use of the material is in the interest of scholarship. In all other instances, however, permission must be obtained from the author of the Thesis.

Name: Addisu Belachew Signature _____ Date: _____

School /Department: Public Health

BIOGRAPHICAL SKETCH

I was born in 1987 G.C in Fitche, North Shewa. I have completed my elementary School in Fitche Number one School. I have attended my Secondary and Preparatory school in Fitche Secondary School (High school). After completion of my Preparatory School I have joined Hawasa University by the year 2005 G.C. At Hawasa University I have studied Nursing and got my first BSC degree on July 2008 G.C.I am serving as Health care provider at Ethiopian Health Insurance Agency, Dire Dwa branch since May 01 /2019 G.C.

ACKNOWLEDGEMENT

I would like to express my gratefulness to Haramaya university college of Health science Instructors for giving me the valuable knowledge for conducting this study. My deepest gratitude goes to my advisorsMr.Tariku Dingeta and Mr. Melake Demena for their insightful and constructive comments.

I would also like to thank Hospital CEO, data collectors, supervisors, and ART service providers working in Dilchora referral hospital for their collaborationduring data collection process.

Finally, I would like to thank my girlfriend Yezihalem Getachew for her support and encouragement throughout my career.I would also like to give special thanks to my friend Mr. Binyam Atnafe for his undeniable support during the period of my study.

ACRONYMES AND ABBREVIATIONS

AIDS	Acquired Immune Deficiency Syndrome
ART	Anti-retroviral treatment
CD4	Cluster of Differentiation 4
CEO	Chief Executive Officer
CI	Confidence Interval
CPT	Cotrimoxazole Prophylaxis Therapy
CSA	Central Statistical Agency
DDRHB	Diredawa regional health bureau
EDHS	Ethiopia Demographic and Health Survey
HAART	Highly Active Antiretroviral Therapy
HAZ	Height for Age Z score
HCA	Head Circumference for Age
HMIS	Health Management Information System
HR	Hazard Ratio
LTFU	Lost To Follow Up
MUAC	Mid-Upper Arm Circumference
OIs	Opportunistic Infections
OR	Odds Ratio
SAM	Severe Acute Malnutrition
TB	Tuberculosis
TO	Transfer Out
WAZ	Weight for age Z score
W/H	Weight for Height

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

ABSTRACT

Background: Early death of children with Human Immunodeficiency Virus (HIV) infected is still high, although they are taking anti-retroviral therapy. However, little evidence was found on predictors of survival time among children living with HIV after initiation of Anti-Retroviral Therapy in Dire Dawa, East Ethiopia.

Objective: Toidentify predictors of survival time among children started antiretroviral treatmentin Dilchora referral hospitalfromJanuary 15, 2019 to February 28, 2019.

Methods: A retrospective cohort study was conducted among eligible children in Dilchora referral hospital started ART from Jan 1, 2012 to Dec 31, 2018. Random sample of 315 medical records included. Data was collected using a pretested data extraction format. It was entered to EpiData software Version 3.1 checked, validated and exported to SPSS Version 23 for analysis using life table, Kaplan Meir test and Cox proportional hazard regression.

Results: Out of 315 reviewed medical records of children, 53(16.8%) died and others censored.The mean age (±standard deviation) of study participants was 90.8(±50.1) months. The mean survival time of the study participants was 68 months (95% CI, 64.3-71.58). Fair/poor ART adherence of children AHR 4.34(95% CI, 1.97-9.58), hemoglobin level less than 10 g/dl(AHR 2.02(95% CI, 1.06-3.87) anddelayed/regressed developmental milestone status (CHR=0.41, 95% CI: 0.19-.90) were associated more likely to die. Children that were presented with WHO staging IV (AHR=4.45, 95% CI, 1.10 -10.80,) and stage III (AHR=3.43, 95% CI, 1.25-9.39) had higher chance of death than those presented at stage (I/II).Risk of death was 3.5 times (AHR=3.55, 95% CI, 1.59- 7.91) higher among patient with CD4 count below threshold.

Conclusion:The meansurvival time of the study participants was 68 months. Fair/poor ART adherence, low hemoglobin level, delayed/regression developmental milestone, higher WHO stage at initiation of ART and low CD4 count were independent predictors of decreased survival time.

Keywords: Human Immunodeficiency Virus, Anti-Retroviral Therapy, Children, Survival time, Dire Dawa

1. INTRODUCTION

1.1. Background

Human Immunodeficiency Virus (HIV) still continues being a public health challenge on human beings, having claimed more than 35 million loss of lives so far globally.HIV pandemic has created unprecedented negative implications on socioeconomic, psychology, culture and health care systems, especially on Sub-Saharan African countries(WHO, 2016).

HIV infection rapidly progresses in children due to different reasons, such as immature immunological status, nutritional factors, clinical and other infections. According to the seventh report of United Nations Children's Fund (UNICEF) in 2016,globally 110,000 number of children (<15 years) and 91,000(80%) is Sub-Saharan are died related to HIV/AIDS cause(UNICEF, 2016).

Ethiopia is one of the hard hit countries in Africa by HIV/AIDS epidemics and has been suffered from related public health challenges. According to the Ethiopian Public Health Institute (EPHI) HIV related estimation and projection for Ethiopia- 2017, there were a total of 722,248 people living with HIV and 57,132 was accounted by children. Annual AIDS death was 14,872 during this period. The estimated children's deaths due to AIDS related illness was 2,607(17.5%) at the same period(EPHI, 2017).

Antiretroviral therapy (ART) has improved the survival time of HIV-infected children by suppression of viral replication in the blood and boosting their immune function through increased CD4 lymphocyte count, decreasing viral load and decreasing other HIV/AIDS-related manifestations(FMOH, 2017).

Ethiopia was among the first few African countries to introduce ART in 2003 in selected health facilities following the national antiretroviral drugs supply and use policy in 2002.The first adult treatment guideline was issued in 2003, and it has been revised in 2005, 2007, 2014 and 2014. Also, a pediatrics treatment guideline was developed in 2007 and the current ART guideline revised in 2017(FMOH, 2017).

Our country started it's free ART program in early 2005 and since then a lot of lives have been saved due to great efforts of the government and its partners. There was different criteria's to initiate ART until 2014 and then Ethiopia launched Test and Treat strategy which enables all people diagnosed with HIV to start ART regardless of clinical staging and CD4 count status(FMOH, 2014).

In our country 1.52%, 0.71% of HIV infected children with ART were dead on 2016 and 2017 respectively. In Dire Dawa city administration there were 578 (in 2016) and 504 (in 2017) HIV infected children on ART. From total death of HIV population 11.3%, 10.8% of were children on 2016 and 2017 respectively(Hapco, 2017).

1.2 Statement of Problem

HIV/AIDS is one of the biggest public health challenge in the world, although there is variation among regions on the level of burden.Since the beginning of epidemic more than 70 million people have been infected and about 35 million died. Globally, 36.9 million people were living with HIV at the end of 2017 and 1.8 million were children. An estimated 110,000 children died due to AIDS-related causes and 82% of these occurred in Sub-Saharan African countries(WHO, 2017).

According to different studies conducted in different parts of the world survival time children on ART is still low.For instance studies conducted in India6% of children died and37% occurred within a month of starting ART and 74% by six months(Jha *et al.*, 2018)in Tanzania 268 children died and 56.3% children died within the first 90 days of ART initiation,(Mwiru *et al.*, 2015),in Ethiopia 4.6 % of children on ART were died (EPHI, 2017),in North Ethiopia 23% of children died after starting anti-retroviral therapy and half (51%) of the deaths occurred within the first 2 years of treatment(Arage *et al.*, 2019), in Adama Referral Hospital and Medical College andmore than three fourth of the deaths occurred in the first six months of ART initiation(Kedir et al., 2014).

According todifferent studies conducted in different placesbeing young age ,underweight, poor adherence andhaving TB co-infection were major factors to shorten survival time of HIV infected children (Habtamu and Eshetu, 2012; Melaku *et al.*, 2017; Sidamo *et al.*, 2017). Also children who started antiretroviral therapy with advanced clinical stages, low hemoglobin level and CD4 cell count below threshold had lower survival time.(Ebissa *et al.*, 2015; Edessa *et al.*, 2015; Mulugeta *et al.*, 2017),(Moy, 2014). However,children are still dying early time after starting Anti-Retroviral Therapy and as far as my knowledge, there is little evidenceon predictors of survival time among children on ART in the study area.

1.3 Significance of the study

This study would bring evidence to fill gap onpediatric chronic HIV care, support and treatment for Dire Dawa City Administration Health Bureau. It might also give insight on regarding existing condition, on predictors of survival time among children on ART to health facilities and health providers.In addition, the generated information will be used for stakeholders (NGO's, HIV associations, etc.) and besides these the study will be used as a baseline for further studies.

1.4. Objectives of the Study

1.4.1 General objective

To identify predictors of survival timeamong children on antiretroviral therapy in Dilchora referral hospital from Jan15, 2019 to Feb 28, 2019.

1.4.2 Specific objectives

To determine mean survival time among children on antiretroviral therapy

To identify predictors of survival time among children on antiretroviral therapy

2. LITERAURE REVIEW

2.1.Survival time of children on ART

The study conducted in Swaziland, South Africa on predictors of survival among children on ART and revealed the mean survival time for children was 78 months (Shabangu et al., 2017).

The mean survival time was found to be 22.4 months with standard deviation of 0.7 months according to a study conducted in Bahir-Dar, Felge-Hiwot referral hospital (Habtamu and Eshetu, 2012) and also other study conducted in this town and the mean survival time was 56.5 months (95% CI:54.62, 58.38 months) and 90.2% of deaths occurred within the first year of treatment (Koye et al., 2012).

A study done in Wolaita zone health facilities , Southern Ethiopia revealed that the mean survival time of HIV infected children on ART was 89.3 months (Bitew et al., 2017). Another study conducted in Mekelle hospital, Northern Ethiopia, on predictors of mortality among HIV infected children on ART reported 55% and 45% of death happened at 12 and 9 months of ART initiation respectively(Gebremedhin *et al.*, 2013).

According study done at Adama Referral Hospital, Ethiopia ,the estimated cumulative survival probabilities were 0.939,0.928,0.926,0.923,0.920,and 0.916 at 6,12,18,36,48 and 60 months respectively, and more than three fourth of deaths occurred within the first 6 months of starting ART (Kedir et al., 2014).

Another study conducted in public hospitals, Addis Ababa, Ethiopia and displayed the cumulative survival probabilities of children after 3,6,12,24,36,48 and 72 months of ART were 0.975, 0.971, 0.958, 0.949, 0.94, 0.935 and 0.931, respectively(Mulugeta *et al.*, 2017).

According to study done in public health facilities of Arba Minch Town, Gamo Gofa Zone, Southern Ethiopia, overall mean estimated survival time of the children was 82.3 months with (95% CI:79.48-85.14) after ART initiation. The cumulative probability of survival at the end of 6th, 12th, 24th, 60th and 96th month was 96.6%, 95.9%, 93.4%,82.9% and 73.9% respectively (Sidamo et al., 2017).

A study also conducted in Hiwot-Fana Specialized University hospital and Jugol hospital, Eastern Ethiopia, among HIV infected children and reported from total death of children 64.3% were died within 6 months of ART initiation (Edessa *et al.*, 2015).

2.2. Predictors of survival time of children on ART

HIV/AIDS continues to be a major public health problem in developing countries especially in Sub-Saharan African countriesand mainly linked on maximizing early death of HIV infected children((UNICEF), 2016). Even though multiple factors are associated with mortality of children in study of Malaysia, nutritional status was an important determinant of survival. The baseline weight for age *z* score ($P< 0.007$) and baseline height for age *z* score ($P< 0.01$) for children who died within the first year of ART initiation were much lower compared with those who did not die in the first year of ART (Moy, 2014).

Mortality was highest among infants (86 per 1000 child years) by the cohort study conducted on Survival of Children Living with Human Immunodeficiency Virus on Antiretroviral Therapy in Andhra Pradesh, India (Jha *et al.*, 2018).

A study in Tanzania compared children with weight for age (WAZ) >−1, those with WAZ ≤−2 to <−3 had a nearly double risk of death (RR, 1.85 (95% CI, 1.10–3.11), and among those with WAZ ≤−3, the risk more than tripled (RR, 3.36 (95% CI, 2.12–5.32) (Mwiru et al., 2015).

A study done in Nigeria and showed HIV infected children with severe wasting (AHR: 5.1; 95% CI: 2.6–9.8) were 5.1 times more likely dead than non-severe wasted (Chamla et al., 2015).Another study in Zambia identified children who had severe acute malnutrition (SAM) 3.8 times more likely died than who have no SAM (3.8; 2.1–6.8) and weight for age (WAZ) <_3 (3.1; 1.6–5.7). This study also revealed total case-fatality rate of SAM was 5.6%, above the Sphere standard (Moramarco et al., 2016).

According to a study done in Swaziland, South Africa, children with HIV after starting ART with the age less than 1 year had 1.55 times higher hazard of death (HR=1.55,95% CI:1.16-2.08), (p <0.001) than children with age group of (1-14) (Shabangu et al., 2017).

A study done in Mekelle Hospital showed that, children with age below 18 months during initiation of ART were 4.39 times more likely to die than elders (AHR=4.39, 95% CI :1.15-17.41) (Gebremedhin *et al.*, 2013).

Another study done in Oromia region around Addis Ababa (Burayu,Holeta, Sebeta and Sendafa) which analyzed a routinely collected HIV care and treatment data and reported that children younger than two years of age had higher risk of death compared to older children(AHR=2.3,95%CI:1.5-3.5) (Melaku *et al.*, 2017).

According to a study done in Adama referral hospital, children who were underweight at baseline 2.49 times more likely to die than children without underweight (AHR=2.49,95% CI:1.27,4.88) (Kedir et al., 2014).

Another study in Addis Ababa confirmed that children on ART with severe underweight more died than moderate and severe; (AHR=10.10;95%CI:2.08,28.00;P=0.004) and (AHR:46.69;95% CI:9.26,200.45;P<0.001) respectively (Ebissa et al., 2015).

According to study done in Adama referral hospital HIV infected children on ART and who had underweight, 2.49 times more likely to die than children who had no underweight (AHR=2.49, 95% CI1.27, 4.88) (Edessa *et al.*, 2015).

Another study done in Wolaita Zone, and showed that HIV infected children after initiation of ART with severe wasting at baseline 7 times more likely to die than do not have nutritional problem (AHR= 7.040 ,95 % CI, 1.267-39.13) (Bitew et al., 2017).

According to a study conducted in Amhara Region , probability of death of severe stunted children approximately 4 times than non- stunted children(AHR: 3.9, 95% CI: 1.7, 9.4), and also revealed that non-wasted children at base line were rescued from death 3 times compared to severely wasted children (AHR: 3.0, 95% CI: 1.3, 6.9) (Alebel et al., 2018).

A study conducted in Swaziland on survival of children on ART and reported children who were diagnosed with TB at base line were estimated to have 3.81 (95%CI, 2.36 -6.13) times higher hazard of death compared to those who were TB negative (Shabangu et al., 2017).

A study done at Felege-Hiwot Referral Hospital in Bahir-Dar children who started ART from 2007 up to early 2009 71 (27.84%) them died due to acquired immune deficiency syndrome(AIDS), 19 (7.45%) were LTFU and advanced WHO clinical stages were important factors of death. According to this study, at any time during the study period children with a baseline WHO clinical stage III were about 50% less likely to die compared with children in the referent category (stage IV) for WHO clinical stage III (AHR=0.494, 95% CI: 0.290-0.842) (Habtamu and Eshetu, 2012).

According to studies conducted in Hiwot- Fana specialized and Jugol hospitals, Eastern Ethiopia and Arba-Minch Town public health facilities , Gamo-Gofa zone, Southern Ethiopia, HIV infected children with poor adherence at last follow up time to ART 2.17 times (AHR=2.17, 95% CI=1.12-4.79) (Edessa *et al.*, 2015).

According to a study done in Eastern Ethiopia ,regressed study subjects at the treatment initiation were 8.8 times more likely to die than those who were appropriate (AHR= 8.8., 95% CI:1.4 -53.8) (Edessa *et al.*, 2015).

Another study conducted in North West Ethiopia at referral hospital and children with absolute CD4 cell count below the threshold for severe immunodeficiency were 2.24 times more likely die than who have CD4 cell count above threshold (AHR=2.24, 95% CI: 1.07, 4.69) and also explained that children who were not on CPT at baseline (AHR=4.74, 95% CI: 2.17, 10.43) 4.7 times increased risk of death compared to taking CPT. This study also revealed a delayed/regressed developmental milestone at initiation of ART 6.31(95 CI%: 2.52, 15.83) times higher risk of death than appropriate developmental milestone and anemia (hemoglobin level <= 10gm/dl) had approximately 2 times more chance of death than above hemoglobin level >10gm/dl (AHR=2.44, 95% CI: 1.26, 4.73) (Koye et al., 2012).

A study in Mekelle Hospital Hospital reported children on ART with CD4 count below threshold (AHR=2.98, 95% CI: 1.12-7.94) 3 times more likely to death than above threshold, WHO clinical stage (III&IV) (AHR= 4.457, 95% CI: 1.01-19.66) 4.5 more likely die than stage I/II, hemoglobin < 10 g/dl (AHR=3.77,95% CI: 1.29-10.98) 4 times more died than without anemia (Gebremedhin *et al.*, 2013).

Another study in Adama referral hospital reported, children with anemia 2.6 times (hemoglobin level<10g/dl) (AHR=2.60, 95% CI=1.41, 4.84), absolute CD4 cell count below the threshold for severe immunodeficiency 3.55 times (AHR=3.55, 95% CI 1.48, 8.46) and advanced WHO staging (stage IV) 3.08 times (AHR=3.08, 95% CI=1.27, 7.47) more likely to die than who were naive to these abnormalities after initiation of ART (Kedir et al., 2014).

According to a study done in Addis Ababa, Ethiopia 10.4% of children were died and 70% of deaths occurred in the first 6 months of ART initiation. Advanced disease stage (WHO clinical stages III and IV ,HR:10.13,95% CI :2.25,45.58,P=0.003) and hemoglobin level less than 7g/dl (HR: 4.08;95% CI :1.33,12.56,P=0.014)were confirmed as significant independent factors of death (Ebissa et al., 2015).

A retrospective study conducted in Hiwot- Fana Specialized University Hospital and Jugol Hospital in Harar and reported that children with baseline regressing developmental milestone had 8.8 times (ARR 8.8; 95% CI 1.4 - 53.8) and baseline CD4 value below threshold 3.8 times (ARR 3.8; 95% CI 1.2 -12.7) risk of death than appropriate

developmental status and with baseline CD4 above threshold respectively (Edessa *et al.*, 2015).

A study done in Addis Ababa and hazard of death in children with WHO clinical stages III & IV were respectively 3(AHR=3.4;95%CI:1.5,7.4) and 5(AHR=4.8;95%CI:1.9,12.2) times higher than those children who had WHO clinical stages I & II at baseline. And also risk of death with hemoglobin level <10g/dl (AHR=3.3; 95%CI: 1.9, 5.9) was 3 times higher than who had hemoglobin level >10g/dl.CD4 cell count below threshold level (AHR=3.4; 95%CI: 1.8, 6.5) were 3 times more likely to die when compared to above threshold. Poor adherence was also an independent predictor of survival of children after initiation of ART (AHR=2.5,95%CI:0.31,18.2) (Mulugeta *et al.*, 2017).

A study conducted in Arbaminch Town, Gamo Gofa Zone, Southern Ethiopia reported children with delayed developmental milestone 4.42 times (AHR=4.42,95%CI:1.99-9.75) and who were regressing developmental milestone 6 times (AHR=6.0,95% CI=2.88 to 13.45,P=0.001) more likely to die early as compared to appropriate milestone after initiation of ART. This study also revealed that those children with hemoglobin level >10g/dl had 3 times more likely to survive than hemoglobin <=10g/dl(AHR=3.32, 95% CI=1.83-6.04), absolute CD4 below threshold had 2 times risk of death than above threshold(AHR=2.08, 95% CI=1.15-3.77), fair and poor adherence to ART were 2 times at risk of death (AHR=2.17, 95% CI=1.12-4.79)(Sidamo et al., 2017).

The study conducted in Southern Ethiopia, Wolaita zone at 2017 and explained children with hemoglobin level ≤10 g/dl had 2 times chance of death than with hemoglobin level >10g/dl (AHR=2.27,95%CI:0.62-8.3) (Bitew et al., 2017).

Another study conducted in Amhara Regional Referral Hospitals and according to this children who had <10g/dl hemoglobin level 3.2 times more likely die than who had >= 10g/dl with (AHR: 3.2, 95% CI: 1.4, 7.4) CD4 cell count below the threshold were 5.2 times higher hazard of death (AHR: 5.2, 95% CI: 1.9, 14.1) than children who had CD4 count above threshold and those children with advanced disease stage at initiation of ART were 2.6 times more likely to die (III and IV) (AHR: 2.6, 95% CI: 1.1, 6.6) compared to stage I and II (Alebel et al., 2018).

2.3. Conceptual framework

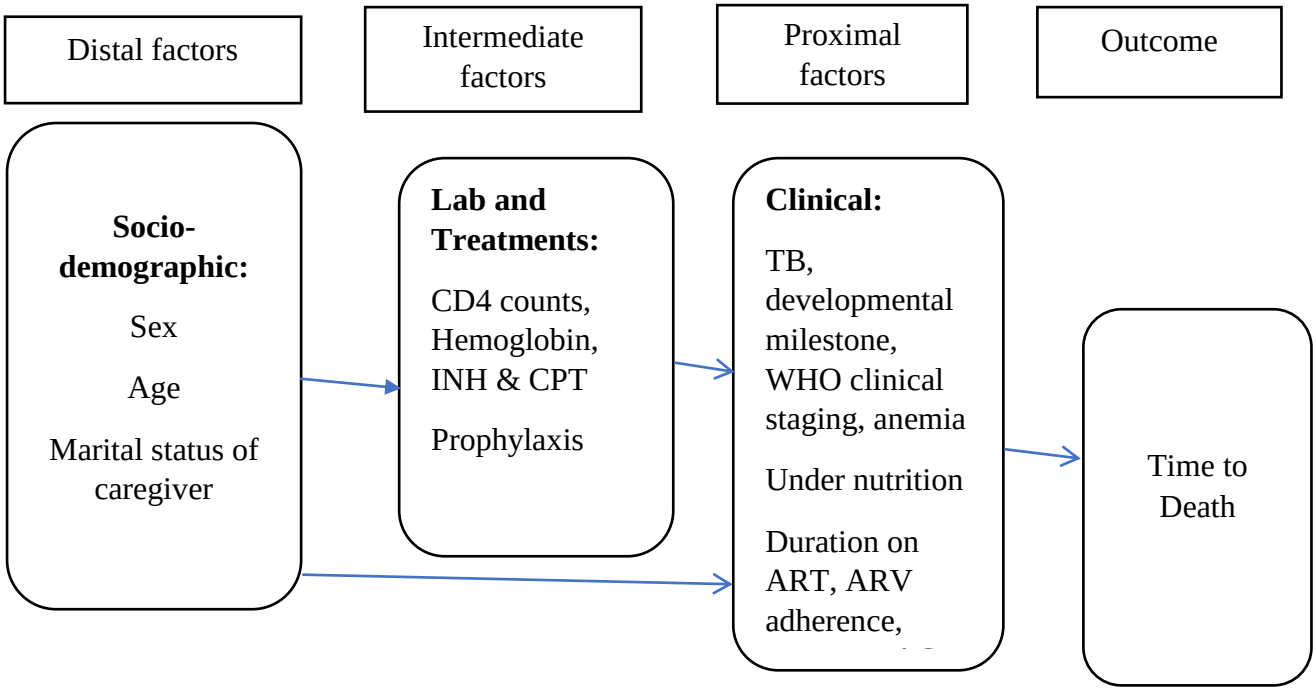

Figure 1Conceptual framework for study of predictors of survival time among children on ART in Dilchora referral hospital Dire Dawa, EastEthiopia (adopted from references) 2019.

3. MATERIALS AND METHODS

3.1 Study Area and Period

This study was conducted in Dire Dawa from January 15, 2019 to February 31, 2019.Dire Dawa is second administrative city located in the Eastern Ethiopia which is about 515 km far from Addis Ababa, at a latitude and longitude 9°36′N and 41°52′E. Dire Dawahas a total population of 453,000 of whom 227,000 are males and 226,000 are females. Administration has 6 hospitals (2 governmental, 4 private hospitals), 15 HC (8 in town and 7 in rural), 34 HP, and 32 private clinics. All hospitals and health centers in town give HIV care.

Dilchora Hospital was established in 1954 and it provides an Outpatient, Inpatient, Chronic care including HIV care and treatment, Gynecology and Obstetrics and other health care services. Besides these, it serves as a referral mainly to Dire Dawa, East Harerghe, Harari and Somali regions.According to Dire Dawa City Administration Health Management Information System(HMIS) 2018 report, the Hospital provide ART service for about 2367 patients and from these patients 11% are children. More than 55% of children and 35% of adult on ART in city administration attend in Dilchora referral hospital (Anonymous, 2017).

3.2. Study Design

A facility based retrospective cohort study was conducted.

3.3. Population

3.3.1. Source Population

All records of children on ARTattended ART clinic in Dilchora Referral Hospital from Jan1, 2012 to Dec 31, 2018.

3.3.2. Study Population

Records ofrandomly selected eligible children attended ART clinic in Dilchora Referral Hospital from Jan1, 2012 to Dec 31, 2018.

3.4. Inclusion and Exclusion Criteria

3.4.1. Inclusion criteria

Records of all children on ART who treated in Dilchora Referral Hospital from Jan 1, 2012 to Dec 31, 2018 were included in the study.

3.4.2. Exclusion criteria

Those medical records that were lost and not able to determine the outcome variable were excluded from study. Records of those children which showed transferred in (TI) were excluded from the study, since it distorts the estimation of outcome variable.

3.5. Sample Size Determination and Sampling Method

3.5.1. Sample size determination

For specific objective one: sample size was calculated using single mean formula

$$N = \frac{(Z\ \alpha\_)^2\ \delta^2}{d^2}$$

2

Where z α/2 =critical value for α level

δ^2 = variability of estimated survival

d =precision level

N =sample size required

Based on previous study estimate of mean survival =56.5 months with standard deviation δ=12 (Koye et al., 2012).

α –error of 5% and precision of 5% (2.8 months)

The calculated sample size n=198

Calculated sample size was = 218

For second objective: sample size was calculated using Stata version 13 (Stata corp., STATA 13.0 for window) for comparing survival Cox model between children had underweight with normal (AHR = 2.42) (Kedir et al., 2014). It was calculated by taking two sided significant level (α) or95 % CI, power 80 %, HR =2.42, probability of event of interest as 0.58 (Kedir et al., 2014).

Table 1: Sample size calculation for association between predictors and survival time of children on ART in Dilchora referral hospital, Eastern Ethiopia, 2019.

Factor considered	Statistics	Sample size	Reference
Anemia (Yes vs No)	AHR =3.77 Probability of Death(P) =0.23 Power=0.8	215	(Gebremedhin *et al.*, 2013)
Under weight (Yes vs No)	AHR=2.42 Probability of Death(p) =0.58 Power= 0.8	324	(Kedir et al., 2014)

Then the total sample size to detect the association between predictors and time to death was 324. Comparing for the first and second objective, then final sample size became 324.

3.5.2 Sampling Technique

Study subjects were selected by systematic random sampling and lottery method was used to get the first number(starting point) and every number next to random number was taken as a study participant. If the data in registration book was incomplete the next number was taken as a study subject. All client charts and registers were evaluated who were on ART between Jan1, 2012 to Dec 31, 2018, finally desired sample obtained, where the sampling interval of the average number of children started ART in divided by the number of children's record to be reviewed in hospital.

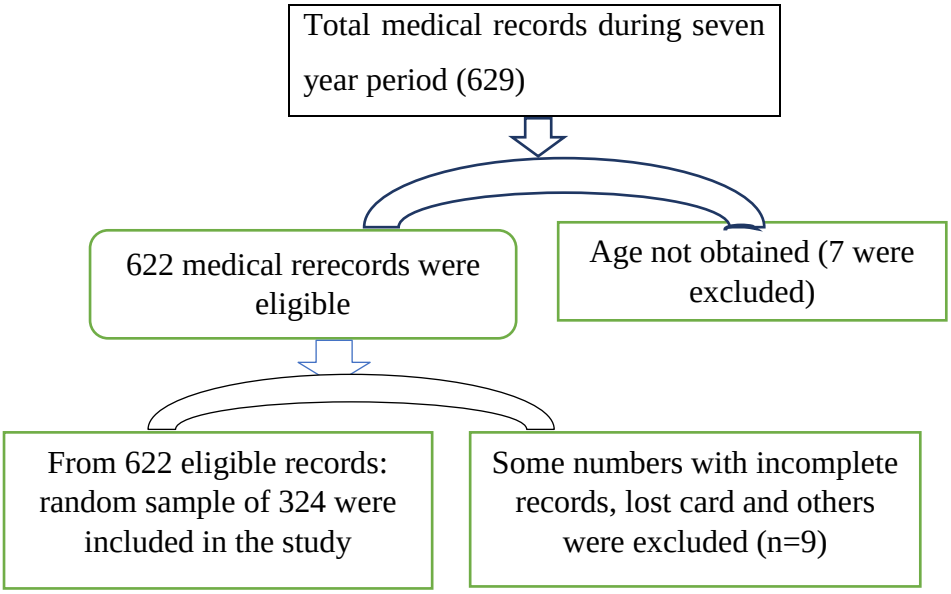

Figure 2 Diagrammatic Scheme of Sampling Procedure, 2019.

3.6. Data Collection Methods

Data collection format was prepared in English. It was adapted from Federal Ministry of Health of Ethiopia ART guideline and ART follow up form. Death was confirmed by reviewing medical registration in the hospital from data base with the help of data clerks. Individuals alive on ART, lost to follow up and transfer out at the end of the study period wereconsidered as censored. Finally, the outcome of each subject dichotomized into censored or death.

3.7. Study Variables

3.7.1. Dependent variable

Time to death

3.7.2. Independent Variables

Socio demographic factors: Age, Sex, marital status

Laboratory measures: Baseline CD4 count, Base line Hemoglobin level

Clinical and Treatments: WHO clinical staging, CPT, history of TB

Nutritional status: underweight, wasting, stunting

Baseline developmental milestone status of the child: delayed, regression, appropriate

3.8. Operational Definition

Wasting: Wt/Ht < -2 Z- score, severe wasting if < -3 Z- score(WHO, 2006)

Underweight: Wt/Age< -2 Z- score, severe underweight if < -3 Z- score(WHO, 2006)

Stunting: Ht/Age< -2 Z- score, severe stunting if < -3 Z- score(WHO, 2006)

Developmental milestone status: ability that has special importance in the growth, motor functioning and social development of children with comparable age(WHO, 2006).

Delayed: if child fails to attain milestones for age; regressed, if a child loses what has been attained for age(WHO, 2006).

Low hemoglobin level: Hgb <11g/dl for age 6-59 months ;< 11.5g/dl for 5 to 12 years; and <12 g/dl for 12 to 15 years(MOH, 2017).

CD4 count below threshold: is <1500 cells/mm3 for under 1 year age ;< 750 cells/mm3 for 1 to less than 3 years old; <350cells/mm3 for 3 to below 5; and <200 cells/mm3 for children aged 5 to below 15 (WHO, 2006).

Children = who are age less than 15 years old and initiated on ART(WHO, 2015).

Lost to follow up = if child discontinued ART for at least 1 to 3 months(WHO, 2015).

3.9. Data Quality Control

Data were extracted from patient/client charts using a standard format. Data were collected by record review using four Nurses. Data collectorsand supervisorswere trained for two days by principal investigator about the objective of the study and data collection methods. The principal investigator and supervisor closely monitored and supervised the whole data collection process on a daily basis. Besides these, there was random checking of data to cross check quality of the collected data. Data's collected from 315 patient records were reviewed and checked for completeness on daily basis and corrective measures were taken as necessary.

3.10. Data Processing and Analysis

Data were cleaned and edited before analysis. Data exploration were undertaken to see if there were odd codes or items that would not be logical and then subsequent editing was made.

Data were entered using Epi-data 3.1 and analyzed by SPSS version 23 for computing simple descriptive statistics including mean, standard deviation and frequency to summarize categorical variables. Association between the outcome and independent variables was taken as significant at $P < 0.05$. Nutritional status was defined by WHO Anthros plus software for generating Z- score of stunting (height for age Z score < -2), Wasting (weight for height Z score - 2) and underweight (weight for age Z score < -2). Univariate analysis was used to describe patient's baseline characteristics.Kaplan Meier was used to test the significance of the observed difference in survival (time to death) curves between each grouped factor.Actuarial table was used to estimate survival after initiation of ART and log rank test was used to compare survival curves across different groups of covariates. Cox proportional-hazard regression was used to calculate the bivariate (crude) and adjusted hazard ratio and then determined independent predictors.Multivariate cox regression analysis was done after adjusting for confounding (age, sex and nutritional status) and age 1-11 months, advanced WHO clinical stages (III & IV) , hemoglobin level <=10g/dl,CD4 count below threshold, fair/poor adherence, delayed/regression developmental milestone are remained as significant predictors of survival time of children.

3.11. Ethical Considerations

The study was conducted after we obtained the Ethical approval from Institutional Health Research Ethics Review Committee (IHRERC) of Haramaya University, College of Health and Medical sciences and letter of cooperation was written from Harmaya University Directorate to Dilchora Referral Hospital. Before data collection Informed, Voluntary, Written and Signed Consent was obtained from Hospital chief executive officer (CEO) based on the recommended criteria. So data collection was carried out after CEO agreed and signed on thewritten informed voluntary consent form to conduct the study on patient's record. To protect confidentiality of the patients name and other identification information were not used.

3.12. Dissemination of results

Thefinding will be presented as partial fulfillment of the degree of Master of public health to department of public health, college of health science, Haramaya University and alsowill be communicated to Dire Dawa City Administration Health Bureau, Ministry of Health, Dilchora Referral Hospital, stakeholders and concerned Non-Governmental Organizations (NGO's). Effort will be made to publish the study in national and international journals.

4. RESULTS

4.1Socio-demographic, clinical and immunological characteristics

A total of 324 children records who started ART from January 1, 2012 to December 31, 2018 selected in the study and card completeness rate was 97.2%.Finally, 315 children records were followed and analyzed.Among the study participants, 52.1% were males and the rest were females.Children who had both parents were 38.7% and double orphaned were 5.4 %.The mean age (±standard deviation) of the study participants was 90.8(±50.1) months and 12%were aged between 1- 11 months, 17.5%were aged between 12-59 months and72.4% were between 5-14 years (Table 2). At initiation of ART,15.6% children had anemia and 8.6% of children were classified as WHO clinical stage IV. Sixty seven percent of children had CD4 count above threshold, while 32.6% had below threshold at base line.Two hundred fifteen (68.3%) of children were on appropriate developmental milestone, whereas 71(25.1%) were delayedand 50.6% of children had under nutrition and 42.4 % were females. Overall, 81(25.9%) wasted, 88(28.2%) underweight and 41(13.1%) were stunted at initiation of ART (Table 2).

Table 2: Socio-demographic, clinical and immunological characteristics of children on ART in Dilchora referral hospital, Dire-Dawa, Eastern Ethiopia,2019.

Variable	Category	Frequency	Percent (%)
Age category	1-12 months	32	10.2
	12-59 months	55	17.5
	60-168 months	228	72.4
Marriage status	Single	82	26.0
	Married.	111	35.2
	Divorced	80	25.4
	Widowed	42	13.3
TB at baseline	Yes	51	16.5
	No	263	83.5
WHO clinical staging	Stage I	123	39.0
	Sage II	77	24.4
	Stage III	88	27.9
	Stage IV	27	8.6
Cotrimoxazole	Yes	180	58.1
	No	135	42.8
Isoniazid	Yes	136	43.2
	No	179	56.8
Developmental	Appropriate	215	68.3
	Delayed	79	25.1
	Regression	21	6.7
Adherence	Good	221	70.2
	Fair	52	16.5

	Poor	42	13.3
Hemoglobin	<=10g/dl	49	15.6
	>10g/dl	266	84.4
CD4	Above threshold	213	67.6
	Below threshold	102	32.4
Underweight	Yes	88	27.9
	No	227	72.1

4.2 Survival status of children

Among 315 children followed on ART, 180(57.1%) were alive, 53(16.8%) were died, 32(10.2%) were lost and 50(15.9%) were transferred out.Out of 53 case of deaths, 27(51%) of children died before 12 months of ART initiation. The mean survival time of the study was 68 months (95% CI 64.3-71.58). After initiation of ART, the minimum follow up time was 1 month and maximum was 96.The mean(±standard deviation) follow up time was 32.35(±23.2).The estimated mortality rate was 6% and 14% at 6 and 78 months of ART initiation respectively.

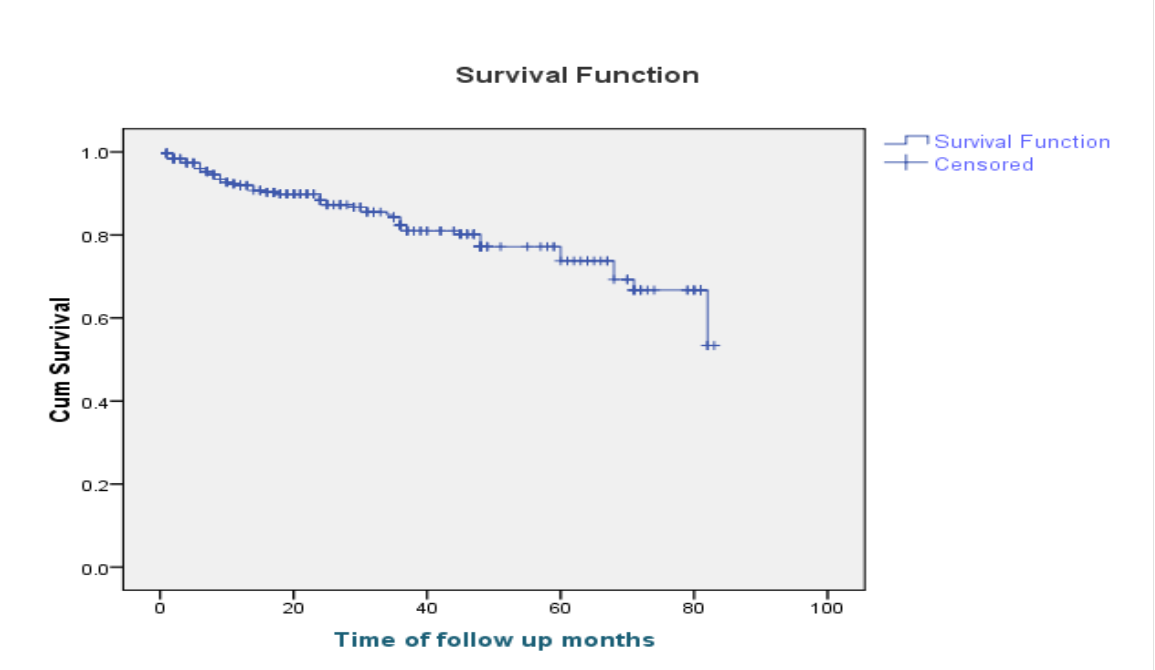

Figure 3 Kaplan Meier survival curve among children on ART in Dilchora referral hospital, Dire Dawa, East Ethiopia, 2019.

Table 3: Life table showing estimation of progression to death of children on ART, Dilchora referral hospital, Dire-Dawa, East Ethiopia, 2019.

Interval Start Time	Number Entering Interval	Number Withdrawing during Interval	Number Exposed to Risk	Number of Terminal Events	Proportion Terminating	Proportion Surviving	Cumulative Proportion Surviving at End of Interval
0	315	24	303.000	8	.03	.97	.97
6	283	26	270.000	15	.06	.94	.92
12	242	35	224.000	4	.02	.98	.90
18	203	22	192.000	1	.01	.99	.90
24	180	21	169.500	6	.04	.96	.87
30	153	9	148.500	2	.01	.99	.85
36	142	23	130.500	6	.05	.95	.82
42	113	24	101.000	2	.02	.98	.80
48	87	25	74.500	2	.03	.97	.78
54	60	10	55.000	0	.00	1.00	.78
60	50	12	44.000	0	.00	1.00	.78
66	38	5	35.500	3	.08	.92	.71
72	30	14	23.000	3	.13	.87	.62
78	13	12	7.000	1	.14	.86	.53

4.3 Predictors of child survival Time

In bivariate analysishavingage between 1-11 months, being widowed, TB co-infection,advanced WHO clinical stages (III & IV) , hemoglobin level <10g/dl,CD4 count below threshold, fair/poor adherence, delayed/regression developmental milestone and underweight at initiation ART were independent predictors of survival time of children. In addition, those study participants who took Isoniazid and Cotrimoxazoleprophylaxis had better survival time. Therefore,the above were considered as candidate for multivariate analysis (P-value< 0.2)(Table 4).

Table 4: Bivariate cox regression of children on ART, Dilchora hospital, East Ethiopia, 2019.

Variable	CategoryDead	Censored	CHR (95% CI)	P-value	
Sex	Male	31(58.5%)	133(50.8%)	1.0	
	Female	22(41.5%)	129(49.2%)	1.458(0.845-2.514)	0.779
Parent presence	Both alive	19(35.8%)	103(39.3%)	1	
	Maternal orphan	13(24.5%)	100(38.2%)	1.072 (0.248-4.634)	0.755
	Paternal orphan	17(32.1%)	46(17.6%)	1.127 (0.259-4.907)	0.779
	Doubleorphan	4(7.5%)	13(4.9%)	2.291 (0.528-9.947)	0.200
Marriage	Single	19(35.8%)	61(23.3%)	1	
	Married	10(18.9%)	101(38.5%)	2.628(0.868-7.960)	0.076
	Divorced	21(39.6%)	59(22.5%)	1.294 (0.398-4.210)	0.669
	Widowed	3(5.7%)	39(14.9%)	3.125 (1.066-9.164)	0.087*
Age	1-11 month	12(22.6%)	20(7.6%)	1	
	12-59 months	16(30.2%)	39(14.9%)	3.464(1.646-7.290)	0.001*
	60-168 months	25(47.2%)	203(77.5%)	3.820 (1.944-7.507	0.000*
CPT	Yes	32(60.4%)	148(56.5%)	1	
	No	21(39.6%)	114(43.5%)	1.629(0.824-3.220)	0.160*
INH prophylaxis	Yes	9(17%)	123(46.9%)	1	
	No	44(83%)	135(53.1%)	2.272(1.163-4.435)	0.016*
History of TB	No	33(62.3%)	231(88.2%)	1	
	Yes	20(37.7%)	31(11.8%)	2.235(1.234-4.047)	0.008*
Clinical Staging	I/II	11(20.8%)	192(73.3%)	1	
	III	29(54.7%)	56(21.4%)	6.859(2.743-7.15)	0.000*
	IV	13(24.5%)	14(5.3%)	11.68(3.99-55.24)	0.000*
Hemoglobin	>10g/dl	29(54.7%)	236(90.0%)	1	
	<=10g/dl	24(45.3%)	26(10%)	5.85(3.34-10.25)	0.000*
CD4	Above threshold	10(18.8%)	204(77.9%)	1	
	Below threshold	43(81.2%)	58(22.1%)	0.179(0.084-0.383)	0.000*

Adherence	Good Fair/poor	4(7.5%) 51(96.2%)	181(69.6%) 79(30.4%)	1 0.348(0.173-0.699)	 0.003*
Milestone	Appropriate Delayed/regression	9(17%) 44(83%)	208(80%) 5(20%)	1 2.278(1.060-4.893)	 0.035*
Under weight	Yes No	26(49.1%) 27(50.9%)	50(19.1%) 212(80.9%)	2.06(1.07-3.97) 1	0.030*

* Statistically associatedpredictor of survival (P < 0.2).

The hazard death of childrenamong age group 1-11 months was almost 3 times and 4 times higher than those 12-59months (AHR= 3.46, 95% CI: 1.64-7.29) and 60-168months(AHR=3.82, 95% CI: 1.94-7.50,P-value<0.001)respectively. Children with hemoglobin level >10g/dl had 2times lower risk of death than with hemoglobin level of <= 10g/dl(AHR= 2.02, 95% CI: 1.06-3.87). Children on ART with CD4 count below threshold(AHR= 3.55, 95% CI: 1.59-7.91) were 3.5 times more likely to die than CD4 count above threshold.Children with fair/poor adherence (AHR=4.34, 95%CI :(1.97-9.58) were 4 times more likely to die as compared to good adherence.Children on ART with delayed/regressed developmental milestone status were59% more likely to die than children with appropriate developmental milestone status (AHR=0.41, 95% CI: 0.19-.90). Children at initiation of ART that were presented with advanced WHO clinical staging IV had almost 4 times (AHR=4.45, 95% CI: 1.10-10.80) and 3 timesIII (AHR=3.43, 95% CI: 1.25-9.39) higher risk of death as compared to clinical stage I/II respectively (Table 5).

Table 5: Multivariate cox regression of children on ART, Dilchora hospital, Dire Dawa, East Ethiopia, 2019.

Covariate	Category	Dead	Censored	CHR (95% CI)	AHR (95% CI)	P-value
Age	1-11 months	12(22.6%)	20(7.6%)	1	1	
	12-59 months	16(30.2%)	39(14.9%)	3.464(1.646-7.290)	3.99(1.52-10.47)	0.005*
	60-168 months	25(47.2%)	203(77.5%)	3.820 (1.944-7.507	4.78 (2.33-9.80)	< 0.001*
INH prophylaxis	Yes	9(17%)	123(46.9%)	1	1	
	No	44(83%)	135(53.1%)	2.272(1.163-4.435)	1.69(0.72-3.94)	0.221
History of TB	No	33(62.3%)	231(88.2%)	1	1	
	Yes	20(37.7%)	31(11.8%)	2.235(1.234-4.047)	1.09(0.54-2.19)	0.794
Clinical Staging	I/II	11(20.8%)	192(73.3%)	1	1	
	III	29(54.7%)	56(21.4%)	6.859(2.743-7.15)	3.43(1.25,9.39)	0.016*
	IV	13(24.5%)	14(5.3%)	11.68(3.99-55.24)	4.45(1.10,10.80)	0.033*
Hemoglobin	>10g/dl	29(54.7%)	236(90.0%)	1	1	
	<=10g/dl	24(45.3%)	26(10%)	5.85(3.34-10.25)	2.02(1.06-3.87)	0.032*
CD4	Above TH	10(18.8%)	204(77.9%)	1	1	
	Below TH	43(81.2%)	58(22.1%)	0.179(0.084-0.383)	3.55(1.59-7.91)	0.002*
Adherence	Good	2(3.8%)	181(69.6%)	1	1	
	Fair/poor	51(96.2%)	79(30.4%)	0.348(0.173-0.699)	4.34(1.97-9.58)	0.003*
Milestone	Appropriate	9(17%)	208(80%)	1	1	
	Delayed/regression	44(83%)	5(20%)	2.278(1.060-4.893)	0.41(0.19-0.90)	0.027*
Under weight	Yes	26(49.1%)	50(19.1%)	2.06(1.07-3.97)	1.21(0.64-2.26)	0.550
	No	27(50.9%)	212(80.9%)	1	1	

* Statistically significant predictor of survival (P < 0.05).

5. DISCUSSION

The study showed that overall mean survival time was 68 months.Among total children followed on ART, 57.1% were alive, 16.8% were died, 10.2%, were lost and 15.9% were transferred out (TO).It also displayed that fair/poor ART adherence, hemoglobin level (<=10g/dl), age 1-11 months, delayed/regression developmental milestone, WHO stage III or IV and CD4 count below threshold were independent predictors of survival time of children.

The mean survival time of this study was higher than those studies conducted at Bahirdar, Felege-Hiwot Referral Hopital (Habtamu and Eshetu, 2012; Koye *et al.*, 2012). This is also slower than two studies done in Southern Ethiopia, Wolaita and Gamo -Gofa zone (Bitew *et al.*, 2017; Sidamo*et al.*, 2017). These discrepancies might be due to changes in the treatment protocol,new drug regimen and care of children on ART time to time and difference inservice deliveries of hospitals.In this study more than 52% death of children occurred within first year of ART initiation. Finding was approximately in line with studies conducted in Northern Ethiopia, Meklle (Gebremedhin *et al.*, 2013), Bahirdar Felege-Hiwot referral hospital (Koye et al., 2012),Adama referral hospital(Kedir et al., 2014) and Eastern Ethiopia, Hiwot-Fana Specialized University hospital and Jugol hospital (Edessa and Likisa, 2015).This could be due to delayed presentation for treatment and poor management of inflammatory reconstitution syndromes (IRS).

Children < 12 months old were4 and 4.7 times more likely to die as compared to12-59 and 60-168 months respectively. It is supported by studies conducted in Swaziland, South Africa (Shabangu et al., 2017) , North Ethiopia, Meklle (Gebremedhin *et al.*, 2013), WolaitaZone, South Ethiopia (Bitew et al., 2017) and India(Jha *et al.*, 2018).Absolute CD4 count below threshold was significantly associated with survival time of children (AHR=3.55, 95% CI: 1.59, 7.91). It is agreed with studies conducted on different parts of Ethiopia (Koye *et al.*, 2012; Gebremedhin *et al.*, 2013; Kedir *et al.*, 2014; Mulugeta *et al.*, 2017). However, finding

almost reduced by half, compared to a study conducted in India (Jha *et al.*, 2018)(AHR: 6.3, 95% CI: 3.5-11.4) and it might be due large sample size of Indian study.

Risk of death in children with hemoglobin level <10g/dl (AHR=2.02; 95% CI: 1.06, 3.8) was 2 times higher than those who had hemoglobin level >10g/dl. This is consistent with reports in Wolaita, Southern Ethiopia (AHR=2.27,95%CI:0.62-8.3) (Bitew et al., 2017), and Bahir-Dar, North West Ethiopia (AHR=2.44, 95% CI: 1.26, 4.73) (Koye et al., 2012). However, it is lower than studies conducted in Mekelle (AHR=3.77,95% CI: 1.29-10.98) (Gebremedhin *et al.*, 2013), Adama referral hospital (AHR=2.60, 95% CI:1.41, 4.84) (Kedir et al., 2014) Addis Ababa (AHR=4.08;95% CI:1.33,12.56) (Ebissa et al., 2015), Arbaminch (AHR=3.32, 95% CI=1.83-6.04) (Sidamo et al., 2017) and Addis Ababa (AHR=3.4; 95%CI: 1.8, 6.5) (Mulugeta *et al.*, 2017). This variation could be due to malaria prevalence of the specific area, Cotrimoxazole prophylaxis therapy coverage and management of its side effect and status of WHO clinical stages of children at initiation of ART and malnutrition.Children who initiated ART at advanced WHO clinical stage III and IV were associated with the reduced survival of children 3.4(1.2, 9.3), 4.4(1.1, 10.8) respectively. It is in line with studies (Kedir et al., 2014) _Adama, (Gebremedhin *et al.*, 2013) _ Mekle (Ebissa et al., 2015) (Mulugeta *et al.*, 2017)._Addis Ababa.However,it is larger than a study in Tanzania(Mwiru et al., 2015) stage III (RR =1.85, 95% CI, 1.05–3.27) and IV (RR= 2.4, 95% CI, 1.3–4.4).There might be variation in treatment approach, guideline protocol and standard of care.

Children with poor/fair adherence were 4 times more likely died than who were good adherence, (AHR=4.3, 95%CI: 1.9, 9.5). This is in line with findings inEastern Ethiopia, Hiwot Fana Specialized University Hospital (HFSUH) and Jugol Hospital (JH), Harar (AHR=2.17, 95% CI=1.12-4.79)(Edessa and Likisa, 2015), and Arbaminch town (AHR=2.05, 95% CI=1.02-4.13) (Sidamo et al., 2017) Southern Ethiopia, Wolaita zone (AHR= 8.9,95%, CI: 2.6-33.7) (Bitew et al., 2017), Addis Ababa (AHR=2.5,95%, CI:0.31,18.2) (Mulugeta *et al.*, 2017).

In this study children with appropriate developmental milestone had 59% less likelychance of death as compared to delayed or regressed (AHR=0.41, 95% CI: 0.18, 0.86). It is lower than those studies conducted in Bahirdar (AHR=6. 95%CI: 2.5 15.8), Harar (AHR=9, 95% CI: 1.4, 53.8), (Koye *et al.*, 2012; Edessa *et al.*, 2015) and Gamogofa Zone, Arbaminch town (AHR=5.95%CI:2.0,9.7) (Mulugeta *et al.*, 2017).It might be explained by delayed or regression complicate the immunological and clinical recovery, prevalence of malnutrition.

Strength of study

The strength of this study is the use of standard check lists which 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, the availability of data on useful predictors of survival time (CD4 count, hemoglobin, and adherence status) were the strongest side of this study.

Limitation

- Using secondary data have incompleteness problem
- Selection bias is possibly introduced during secondary data collection
- Mortality might beunderestimated as the considerable number of children lost to follow up may include children who died.

6. CONCLUSION AND RECOMMENDATION

6.1 Conclusion

In this study 53 children died after starting antiretroviral treatment during study period. The mean survival time of children on ART was 68 months and also, 27(51%) of children died before 12 months of ART initiation. Fair/poor ART adherence, hemoglobin level (<=10g/dl), age 1-11 months, delayed/regression developmental milestone, WHO stage III or IV and CD4 count below threshold at initiation of ART were independent predictors of survival of children.

6.2 Recommendations

- Follow up of children on ART should be strengthen by program planners and other stakeholders in Dire Dawa.
- Health workers in Dilchora referral hospital and other health facilities in Dire Dawa need to give more emphasis for children with advanced WHO clinical stage, delayed or regressing developmental milestone, poor adherence, infants, anemia, CD4 count below threshold during ART initiation.

7. REFERENCE

(UNICEF). (2016). "FOR EVERY END AIDS Seventh Stocktaking Report, 2016." from https://www.unicef.org/publications/index_93427.html.

Alebel, Wagnew, Tesema, Kibret, Petrucka and Eshite (2018). "Effects of undernutrition on survival of human immunodeficiency virus positive children on antiretroviral therapy." Italian Journal of Pediatrics.

Anonymous (2017). Federal Democratic Republic of Ethiopia Central Statistical Agency Population Projection of Ethiopia for All Regions: At Wereda Level from 2014 - 2017. Addis Ababa, Federal Ministry of health**:** 70-90. .

Arage, Assefa, Worku and Semahegn (2019). "Survival rate of HIV-infected children after initiation of the antiretroviral therapy and its predictors in Ethiopia: A facility-based retrospective cohort." *SAGE Open Medicine***7**: 8.

Bitew, Mekonen and Assegid (2017). "Predictors on mortality of human immunodeficiency virus infected children after initiation of antiretroviral treatment in Wolaita zone health facilities, Ethiopia:Retrospective cohort study." Journal of AIDS and HIV Research.

Chamla, Asadu, Davies, Wagt, Ilesanmi4, Adeyinka and Adejuyigbe (2015). "Patching the gaps towards the 90 90 90 targets: outcomes of Nigerian children receiving antiretroviral treatment who are co-infected with tuberculosis." Journal of the International AIDS Society**18**.

Ebissa, Dyessa and Biadigilign (2015). "Predictors of early mortality in a cohort of HIV-infected children receving high active antireroviral treatment in public hospitals in Ethiopia." PubMed.

Edessa, Asefa and sheikahmed (2015). "Early Mortality among HIV-positive Children Initiated Anti-Retroviral Therapy in Eastern Ethiopia: A Retrospective Cohort Study." STAR JOURNAL.

Edessa, Asefa and **sheikahmed** (2015). Early Mortality among HIV-positive Children Initiated Anti-retroviral Therapy in Eastern Ethiopia: A Retrospective Cohort Study. Science, Technology and Arts Research Journal.

Edessa and Likisa (2015). "A Description of Mortality Associated with IPT plus ART Compared to ART Alone among HIV-Infected ndividuals in Addis Ababa,Ethiopia: A Cohort Study." PLOS ONE.

EPHI. (2017). "HIV Related Estimates and Projections for Ethiopia-2017 ", from https://www.pepfar.gov/documents/organization/272012

FMOH. (2014). "CONSOLIDATED GUIDELINE." from www.who.int.

FMOH. (2017). "National Guidelines for Comprehensive HIV Prevention, Care and Treatment." from https://www.google.com/search?q=NATIONAL+GUIDELINES+FOR+COMPREHENSIVE+HIV+PREVENTION%2C+CARE+AND+TREATMENT&oq.

Gebremedhin, Gebremariam, Haile, Weldearegawi and Decotelli (2013). "Predictors of mortality among HIV infected children on anti-retroviral therapy in Mekelle Hospital, Northern Ethiopia: a retrospective cohort study." BMC Public Health.

Habtamu and Eshetu (2012). "Factors affecting the survival of HIV-infected children after ART initiation in Bahir-Dar, Ethiopia " *Ethiop. J. Health Dev.* .

HAPCHO. (2017). "HIV Epidemic Estimates 2017-2021,Ethiopia." from <http://www.aarc.gov.et/aarc/images/demo1/Ethiopia%20collection/HIV%20Epidemic%20Esti>.

Jha, Dhingra, Raj, Rewari, Jeyaseelan, Harvey, Chavan, Saggurti and Reddy (2018). "Survival of Children Living with Human Immunodeficiency Virus on Antiretroviral Therapy in Andhra Pradesh, India." INDIAN PEDIATRICS.

Kedir, Desta and Fesseha (2014). "Factors Affecting Survival of HIV Positive Children Taking Antiretroviral Therapy at Adama Referral Hospital and Medical College, Ethiopia." AIDS & Clinical Research Open access journal(1000289).

Koye, Ayele and Zeleke (2012). "Predictors of mortality among children on Antiretroviral Therapy at a referral hospital,Northwest Ethiopia: A retrospective follow up study." BioMed Central(161).

Melaku, Lulseged, Wang, Lamb, Gutema, Teasdale, Ahmed, Gadisa, Habtamu, Bedri, Fayorsey and Abrams (2017). "Outcomes among HIV-infected children initiating HIV care and antiretroviral treatment in Ethiopia." Tropical Medicine and International Health.

MOH. (2017). "MINISTRY OF HEALTH, E. (2017) National Comprehensive HIV Prevention, Care and Treatment Training for Health care Providers
", from <https://aidsfree.usaid.gov/sites/default/files/resources/ethiopia_art_guidelines_2017.pdf>

Moramarco, Amerio, Ciarlantini, Chipoma, Simpungwe, Nielsen-Saines, Palombi and Buonomo (2016). "Community-Based Management of Child Malnutrition in Zambia: HIV/AIDS Infection and Other Risk Factors on Child Survival." International Journal of Environmental Research and Public Health.

Moy (2014). "Outcomes of human immunodeficency virus-infected children after anti-retroviral therapy in Malaysia." J Peadtric Child Health.

Determinants of Survival among HIV Positive Children on Antiretroviral Therapy in Public hospitals, Addis Ababa, Ethiopia " Insight Medical Publishing Group

Mulugeta, Assefa, Tewelde and Dube (2017). "Determinants of Survival among HIV Positive Children on Antiretroviral Therapy in Public hospitals, Addis Ababa, Ethiopia " Insight Medical Publishing Group

Mwiru, Spiegelman, Duggan, Seage, Semu, Chalamilla, Kisenge and Fawzi (2015). "Nutritional Status and Other Baseline Predictors of Mortality among HIV-Infected Children Initiating Antiretroviral Therapy in Tanzania." Journal of the International Association of Providers of AIDS Care.

Shabangu, Beke, Manda and Mthethwa (2017). "Predictors of survival among HIV-positive children on ART in Swaziland." African Journal of AIDS Research: 10.

Sidamo, Debere, Enderis and Abyu (2017). "Incidence and Predictors of Mortality among Children on Anti-RetroviralTherapy in Public Health Facilities of Arba Minch Town, Gamo Gofa Zone, Southern Ethiopia; Retrospective Cohort Study." Clinics in Mother and Child Health(3 • 1000267).

UNICEF (2016). " UNICEF(2016) HIV and AIDS Seventh Stocktaking Report 2016."

WHO. (2006). "WHO(2006) the WHO growth standards." from https://www.who.int/childgrowth/standards/Technical_report.pdf

WHO. (2015). "Guideline on when to start antiretroviral therapy and on pre-exposure prophylaxis for HIV " WHO, from www.who.int/hiv.

WHO. (2016). "Global AIDS response progress reporting 2016." from aidsreportingtool.unaids.org

WHO. (2017). "WHO (2017) Global AIDS response progress reporting 2017." from https://www.unaids.org/sites/default/files/media_asset/20170720_Data

ANNEX

Annex I:Information Sheet

1. The study/project title:

Survival status and associated factors among HIV Infected children on ART in Dilchora Referral Hospital in Dire Dawa, Eastern Ethiopia.

2. Purpose/aim of the study:

The findings of this study can be of a paramount importance for the Hospital to plan intervention programs to prevent first line antiretroviral treatment failure in the community and others; thereby improve potent use of first line antiretroviral treatments in general. Moreover, the aim of this study is to write a thesis as a partial requirement for the fulfillment of a Master's Program in Epidemiology for the principal investigator.

3. Procedure and duration:

My data collectors will review patient records of ART clinic using a standard checklist among which HIV infected children <15 will be a candidate for this study to provide me with pertinent data that is helpful for the study. There are questions to answer where the data collectors will fill the questionnaire by reviewing patient records..

4. Risks and benefits:

The risk of conducting in this study is very minimal but taking sometime from ART clinic professionals. There would not be any direct payment for participating in this study, but the findings from this research may reveal important information for the local health planners concerning ART treatment and care.

5. Confidentiality:

The information that we will be provided will be kept confidential. There will be no information that will identify the participants' record in particular. The findings of the study will be general for the study community and will not reflect anything particular of individual persons.

The data collection checklist will be coded to exclude showing names. No reference will be made in oral or written reports that could link participants to the research.

6. Rights:

The manager has the right to allow or stop this study from being conducted in the Hospital. The Hospital also has the right to withdraw from the study at any time and this will not label them for any loss of benefits which they otherwise are entitled.

7. Contact address:

If there are any questions or enquires any time about the study or the procedures, please contact through the following address:

Principal investigator: Addisu Belachew
E-mail: Kasadis2016@gmail.com
Mobile phone: 09-21-86-36-21

Institutional Health Research Ethics Review Committee (IHRERC) of Haramaya University college of Medicine and Health science: Office phone: 0254 66 20 11: P.O.BOX: 235, Harar.

8. Declaration of informed voluntary consent:

I have read the participant information sheet. I have clearly understood the purpose of the research, the procedures, the risks and benefits, issues of confidentiality, the rights of participating and the contact address for any queries. I have been given the opportunity to ask questions for things that may have been unclear. I was informed that the Hospital has the right to stop this study from being conducted in the Hospital if any misdeeds and unethical procedures are observed during the data collection process in the Hospital's premises. Therefore, I declare my voluntary consent on behalf of Dilchora Referral Hospital management to allow this study to be conducted in the Hospital with my initials (signature).

Name and Signature of Head of the Hospital: _____

Name and Signature of Principal investigator: _____

Date _____

Annex II:Data collection format

This is a checklist set to collect information on predictors ofsurvival time among HIV Infected children in Dilchora Referral HospitalDire Dawa, Eastern Ethiopia:

Instruction: First introduce yourself and tell about the objectives of the study then request him/her to review the selected records of HIV infected children. Finally fill all individual information from patient record on the checklist correctly. Please write the required information clearly and completely.

01. Checklist identification number_____
02. Reviewer name_____
03. Date of review_____

Part-I SOCIO DEMOGRAPHIC CHARACTERISTICS

No	Check lists	Possible answers
101	Age of the child	(…….)years or (…….) months
102	Sex of the child	1.Male 2.Female
103	Parent survival status	1. Both parents are alive 2.Maternal orphan 3.Paternal orphan 4. Double orphan
104	Current marital status of parent	1.Single 2.Married 3.Divorced 4.Widowed

Part-II Base line clinical, laboratory and ART information

201	Cotri-moxazole Prophylaxis Therapy(CPT) given	1. Yes 2.No	
202	INH prophylaxis given	1.Yes 2.No	
203	History of TB at baseline?	1. Yes 2.No	
204	WHO staging at baseline	1. Stage I 2. Stage II 3. Stage III 4. Stage IV	
205	Weight at base line	(----------) kg	
206	Height/length at base line	(----------)cm	
207	MUAC at baseline	(……..)cm	
208	BMI for age at base line	(……..)kg/m2	
209	HCA at baseline	……..cm	
210	Hemoglobin at baseline	----------g/dl	
211	Nutritional status at base line	1. Normal 2.wasting 3. Underweight 4.stunting	
			If no

212	Is there severe malnutrition?	1. Yes 2. No	skip
213	If there were severe form of malnutrition	1.Sevre wasting 2.Severeunderweight 3.Severe stunting	
214	Developmental milestone status	1. Appropriate 2.Delay 3.Regression	
215	CD4 count at base line	(---------) date----------/-------/---	

Part- III patient follow up information (filled from ART follow up form) recent results

301	ART started date	----------/----------/-------	
303	Duration since ART initiation or month of ART	…….Months	
304	Recent ARV adherence	1. Good 3. Poor 2.Fair	
305	Last follow up date	----------/----------/--------	
306	Final status of the child	1. Alive 2. Dead 3. LTFU 4.TO	
307	If dead when?	Date of death…… /……. /……. Age of child at death--------yrs. or----------months	

Annex III: Curriculum vitae (CV)

Personal Details

Name: Addisu Belachew

Date of birth: March 18, 1987 G.C

Sex: Male

Marital status: Single

Nationality: Ethiopian

Birth place: Fitche

Contact address: Mobile phone (+251)-9-21-86-36-21

Office: (+251)-025-113-01-01

Email-address: Kasadis2016@gmail.com

Academic background

Level of education	School place
Primary school	Adisge primary school (1986-1989 E.C) and Fitche number 1 school (1990-1993E.C)
High school and Preparatory school	Fitche Secondary and Preparatory school (1994-1997E.C)
BSc in Nursing	Hawassa University (1998-2000E.C)

Work experience

2001 to 2002 E.C Jeldessa health center DDRHB

2002 to Jan 2010 E.C Gende Gerada health center DDRHB in different positions

Jan 2010 E.C Sep 2011E.C ART coordinator/CDC project at Sabian primary hospital

Currently on Ethiopian Health Insurance Agency Dire dawa branch

Basic Trainings

TB/HIV, MDR-TB, Food by prescription, VCT

Consolidated ART, STI, Infection prevention control

Vaccine management, AWD management, surveillance

Nursing leadership, Health ethics, Basic HMIS

References

1. Birhanu Alie (MPH), Lecturer at Haramaya University Health and Medical Scienece College

Mobile: +2519-13-44-28-34

Email:birhanualle@gmail.com

2. Biniam Atnafe (MPH), Curative and rehabilitative case team coordinator at Gende Gerada health center

Mobile: 09-11-39-29-04

Email:Binyamat@gmail.com