Journal of
AIDS & Clinical Research
ISSN: 2155-6113

Kedir et al., J AIDS Clin Res 2014, 5:3
DOI: 10.4172/2155-6113.1000289

Review Article Open Access

Factors Affecting Survival of HIV Positive Children Taking Antiretroviral Therapy at Adama Referral Hospital and Medical College, Ethiopia

Adem Aman Kedir[2], Alem Desta[1]* and Girmatsion Fesseha[1]

[1]Department of Public Health, College of Health Sciences, Mekelle University, Mekelle, Ethiopia
[2]Oromia Regional Health Bureaus, Adama, Oromia, Ethiopia

Abstract

Background: The aim of this study is to explore factors affecting survival of children living with HIV/AIDS after initiation of ART. In which it highlights the need for local evidence to promote interventions that optimize survival among HIV-infected children on ART in Ethiopia.

Methods: Institution based retrospective cohort study was employed on 560 children enrolled on ART from January, 2006-December, 2010. Information on relevant variables was collected from patients` medical cards and registries. Univariate analysis was used to describe the baseline characteristics of the patients`. Life table was used to estimate survival after initiation of ART. Log rank test was used to compare survival between different categories of independent variables. Multivariable Cox proportional model was fitted to identify factors affecting survival after initiation of ART.

Results: Children on ART were followed for a median follow up period of 47 months (IQR=29, 62). At the end of follow up, 364 (65%) were alive and 43 (7.6%) were reported dead. More than three fourth of the deaths occurred within the first sixth months of starting ART. 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. Anemia (hemoglobin level<10 gm/dl) (AHR=2.60, 95% CI=1.41, 4.84), absolute CD4 cell count below the threshold for severe immunodeficiency (AHR=3.55, 95% CI 1.48, 8.46), advanced WHO staging (stage IV) (AHR=3.08, 95% CI=1.27, 7.47), and underweight (AHR=2.49, 95% CI 1.27, 4.88) have found to be predictors of mortality after ART initiation.

Conclusions: Mortality was high especially during the first sixth months following ART initiation. Therefore, close follow up of HIV exposed children to make early diagnosis and treatment initiation before the development of severe immune deficiency and advanced clinical stage is important.

Keywords: Survival status; HIV/AIDS; ART; Children; Adama; Oromia; Ethiopia

Introduction

For three decades, HIV/AIDS has been overwhelming individuals and families with the disaster of untimely death and medical, financial and social burdens. In 2012, globally 3.4 million people living with HIV were children under age of 15 years; and an estimated 250,000 children under age of 15 years were died due to AIDS related cases globally in 2011 [1]. Sub-Saharan Africa, a region with only 12% of the global population; remains the most heavily affected region by HIV. In 2011, about 69% of all people living with HIV and more than 50% of deaths from AIDS-related illnesses in adults and children`s occurred in this area [2].

The development of HIV into AIDS is very rapid in a proportion of infants and children; in the absence of appropriate treatment; a third of children infected with HIV will die before their first birthday [3]. In 2009, about 260,000 deaths due to HIV were reported in under-15 years children; of which a significant number of deaths could have been averted by early diagnosis and treatment [4]. Although the risk of early mortality is high in HIV infected children, the average age of ART initiation in low income countries stayed high [5]. Studies conducted following the recommendation of WHO for ART in infants and children supported that early initiation of ART prevent early mortality [6].

Though survival of HIV positive children in Ethiopia and similar settings has improved as a result of increased access to ART, it is still low in the first six months after initiation of ART [7]. However, studies conducted in Kenya, Zambia, and Malawi; the death of HIV positive children following ART initiation remains high, ranging from 7.5% to 15% [8-10]. Nevertheless, HIV positive children in developed countries have a substantially higher survival probability after initiation of ART compared to children in developing countries [11].

The effect of socio-demographic, clinical and immunological factors on survival of HIV positive children after initiation of ART were also studied in low and middle income countries. However, the findings of the studies were not consistent. For instance, in studies conducted on cohorts of HIV positive children in Cote d`Ivoire, Malawi and Zambia, only low weight-for-height and low CD4% were found to have significant negative effect on survival of children after initiation of ART [7,9,10]. However, in another large cohort of HIV positive children of Zambian, besides low CD4% and low WHZ score, younger age and low hemoglobin level were also found to have significant negative effect on survival after initiation of ART [12].

In addition, the scarcity of data on survival of children receiving ART beyond 2 years of follow up was another reason why this study

***Corresponding author:** Alem Desta, Department of Public Health, College of Health Sciences, Mekelle University, P.O.BOX 1871, Mekelle, Ethiopia, Tel: +251-034-441-66-83; Fax: +251-034-441-66-75; E-mail: wuneha@gmail.com

Received January 30, 2014; **Accepted** March 03, 2014; **Published** March 15, 2014

Citation: Kedir AA, Desta A, Fesseha G (2014) Factors Affecting Survival of HIV Positive Children Taking Antiretroviral Therapy at Adama Referral Hospital and Medical College, Ethiopia. J AIDS Clin Res 5: 289. doi:10.4172/2155-6113.1000289

Copyright: © 2014 Kedir AA, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

conducted. However, in this study the children were followed for longer period to estimate their survival status. Though ART service is being provided since 2005, there are no studies or documented report on survival status and factors affecting survival of children on ART in the study area. This highlights the need for local evidence to estimate the survival status and identify factors affecting survival of children on ART at Adama referral hospital and Medical College. Therefore, the purpose of this study is to determine survival status and identify factors affecting survival of HIV positive children after initiation of ART.

Methods

Study setting and period

The setting for this study was Adama Referral Hospital and Medical College located at the center of Adama Town. Adama town, located at 99 km southeast of Addis Ababa, is an administrative center for East-Shoa Zone in Oromia Regional State. Adama Referral Hospital and medical college was one of the first three hospitals in Oromia that started providing ART services since 2005. HIV infection is confirmed by serological testing or DNA PCR used in infants under 18 months of age. At ART clinic, HIV positive children are screened for opportunistic infections, evaluated for clinical staging and eligibility for ART by ART physician or nurse. Patients were managed in accordance with World Health Organization (WHO) recommendations [13] and national guidelines [14]. The ART case team in the hospital comprised of ART trained physicians; ART trained nurses, pharmacist, laboratory technicians, data clerks, and drug adherence counselors. A total of 1860 children have been enrolled since March 2005, 1350 children ever started on ART and 980 children currently on ART [15]. The study subjects were followed from January 1st 2006 to march 6th 2013.

Study design and sampling

Institution based retrospective cohort study design was conducted. All Children living with HIV/AIDS, age ≤ 14 years and started ART at Adama referral hospital and Medical College were source population for the study. The study population was randomly selected medical records of HIV positive children that were enrolled on ART between January 1st 2006 and 30th of December 2010 at the hospital. The sample size was calculated by applying two sample proportion formula using Epi-Info version 7. The most significant predictors of survival (absolute CD4 count) were used [16]. The calculated sample size was 560. Sampling frame containing 1030 medical card numbers of children living with HIV/AIDS that started ART between January 1st 2006 and 30th of December 2010 was prepared. Then from the sampling frame, the medical cards randomly selected using select cases randomly option in SPSS v.20 statistical software.

Measurements

The data source for this study was medical records of HIV positive children enrolled on ART at Adama Referral Hospital. The time to death was the outcome variable. The time to death was assessed for subjects from the date of ART initiation to the date of death occurring before March 6th, 2013 (end of study period). Children were followed until they died; loss to follow up, transferred to other health facility, or administratively censored on March 6th, 2013. Data on deaths of the HIV positive children on ART were obtained from physician report on the medical cards. Besides, for those children who died at home, the drug adherence counselor communicated using the contact address and confirmed whether the children were alive or dead. Checklist for data collection was adopted from intake and follow up form used in the children ART clinics. Measurements were developed from WHO standards and by reviewing relevant literatures [17-19]. Pre-testing was under taken in Adama health center before data collection and some minor modification were made accordingly. The data was collected by reviewing the patient's medical cards (follow up and ART intake form) from March 1st to 15th, 2013. Three clinical nurses trained on ART were employed for data collection after receiving one day training on the objectives and process of data collection. The most recent laboratory results before starting ART was used as a baseline value. Kaplan-Meier was used to estimate survival after the advent of ART, and log rank test was used to compare the observed survival curves. Those variables with P-value less than 20 percent in log rank test were selected as potential candidate for the multivariable cox proportional hazard model [20]. Purposeful selection of covariates method was used to select variables for the multivariable model. No interaction was found among covariates in the final model. Only independent variables that will have statistically significant association with the outcome variable on multivariable Cox-proportional hazard will be retained in the final model. The Proportional hazard assumption was checked for variables included in the final model using re-estimation based method and none of the variables in the final model violated the proportionality assumption. The overall goodness of model fitness was checked using Cox-snail method. Alpha 5% was used as level of significance. Weight-for-age was calculated using anthropometric calculator of WHO anthro plus software.

The quality of the data was assured by caring out careful design of the check list, pre-test, cleaning of data and appropriate recruitment and training was given for data collectors. Five percent of the completed data collection checklist was selected randomly and cross checked with medical cards of the patients to check for consistency at the end of each day. The collected data was coded, entered, cleaned and analyzed using STATA version 11 statistical package.

Operational definitions

Anemia: was defined as having hemoglobin level below 10 gm/dl.

CD4 count below threshold: was classified according to the age of a child. For infants CD4 count less than 1500/mm^3, For age 12-35 months CD4 count less than 750/mm^3, For age 36-59 months CD4 count less than 350/mm^3, For age ≥ 60 months CD4 count less than 200/mm^3 (38).

Fair adherence: if the percentage of missed dose is between 85-94%

Good adherence: if the percentage of missed dose is above >95%

Lost to follow up: if a patient discontinued ART for at least one to three month.

Regressed developmental milestone: if a child loses what has been attained for age.

Underweight: was defined as weight for age Z-score<-2 SD for under-five children and BMI-for-age score<-2 SD for children ≥5 years old.

Ethical clearance was obtained from the Mekelle University College of Health Sciences, Institutional Research Ethics Review Committee. Following the approval, Official letter of co-operation was written to concerned bodies by the School of Public Health of Mekelle University. Permission was granted from Oromia Regional Health Bureau and Adama referral hospital and Medical College. As the study was conducted through review of medical cards, the individual patients was not exposed to any harm as far as the confidentiality maintained. Moreover, no personal identifier was used on data collection form. The

recorded data was not accessed by a third person except the principal investigator, and kept confidential.

Results

Baseline socio-demographic profile of children

Five hundred sixty (560) medical cards of children living with HIV/AIDS and who started ART were reviewed for this study. Three hundred thirty three (61.5%) were above age 5 years at initiation of ART and those age less than 1 year accounts for 51 (9.1%) of the children. Two hundred seventy seven (49.4%) of the children were males. Four hundred forty one (78.7%) were from urban. Of 499 children whose orphan hood status were recorded, 161(32.2%) of the children have lost either of their parents, (Table 1).

Baseline clinical and immunological profile of children

Immunization status recorded were recorded for 347 HIV positive children; of which 294(84.7%) were vaccinated at appropriate age. Regarding feeding practice, 83(33.4%) HIV positive children were on exclusive breast feeding; whereas 154(62.1%) on mixed feeding. Four hundred twenty (75%) were on cotrimoxazol prophylaxis therapy at ART initiation. Four hundred ninety four (96.5%) of the children found to have good adherence for ART, whereas 10 (2.0%) and 8(1.5%) had fair and poor adherence level, respectively. Three hundred forty nine (62.7%) of the children had absolute CD4 count below threshold for immune deficiency. Of 522 children whose hemoglobin value at initiation were recorded, 109 (20.9%) had anemia (Hgb<10 gm/dl). Two hundred eighty nine (51.6%) of them were malnourished (underweight). Sixty three (11.7%) and 16 (3%) of the children had a delayed and regressed developmental milestone, respectively (Table 2).

Survival analysis

A total of 560 children on ART were followed for a median follow up time of 47 (IQR, 29-62) months. At the end of follow up, 364 (65%) were alive, 46 (8.2%) were loss to follow up, 107 (19.1%) were transferred out and 43 (7.6%) were reported dead. Thirty three (76.7%) of the total deaths have occurred within the first sixth months of starting ART. The overall mortality rate was 2.06 deaths per 100 child-years (43 deaths over a 2078 child-years). The estimated cumulative survival probability was 0.958 after 3 months, 0.939 after 6 months, and 0.920 after 12

Variable	Frequency	Percent (%)
Age category		
<1 year	51	9.1
1-5 years	165	29.4
5-14 years	344	61.5
Sex		
Male	277	49.4
Female	283	50.6
Residence		
Rural	119	21.2
Urban	441	78.8
Care giver (n=551)		
Parents	394	71.5
Grand parents	59	10.7
Siblings	36	6.5
Guardian	46	8.4
Orphanage centers	16	2.9
Orphan hood (n=499)		
Both parents are alive	244	48.9
Maternal orphan	68	13.6
Paternal orphan	93	18.7
Double orphan	94	18.8

Table 1: Baseline socio-demographic characteristics of children started ART at Adama referral hospital and medical college, January 1st, 2006 to December 30th, 2010.

Variable	Frequency	Percent (%)
Immunization (n=347)		
Appropriate for age	294	84.7
Not appropriate for age	41	11.8
Not immunized	12	3.4
Nutritional history (n=248)		
Exclusive Breastfeeding only	83	33.4
Replacement only	11	4.4
Mixed Breastfeeding	154	62.1
Infant prophylaxis (n=189)		
None	171	90.4
sdNVP	7	3.7
sdNVP + AZT	7	3.7
Cotrimoxazol prophylaxis		
Yes	420	75.0
No	140	25.0
ART Adherence on follow up (n=512)		
Good	494	96.5
Fair	8	1.5
Poor	10	2.0
Absolute CD4 count		
CD4 count above threshold	207	37.2
CD4 count below threshold	349	62.7
Hemoglobin (n=522)		
≥ 10 gm/dl	413	79.1
< 10 gm/dl	109	20.9
WHO clinical staging		
Stage I	59	10.5
Stage II	101	18.0
Stage III	330	59.0
Stage IV	69	12.5
Nutritional status		
Under weight	289	51.6
Normal	266	47.4
Over weight	5	1.0
Developmental milestone (n=537)		
Appropriate	458	85.3
Delayed	63	11.7
Regressed	16	3.0
Opportunistic Infections on follow up		
Yes	171	34.0
No	333	66.0
ART drug side effect during follow up		
Yes	38	7.0
No	522	93.0
Previous PTB		
Yes	85	15.0
No	475	85.0

Table 2: Baseline clinical and immunological status of children started ART at Adama referral hospital and medical college, January 1st, 2006 to December 30th, 2010.

months of ART initiation. The cumulative survival after 54 months was 0.916 (Table 3 and Figure 1).

Kaplan-Meier survival curves among categories of the variables

Children on ART who had normal weight for age have significantly higher survival probability compared to those under-weight at ART initiation (log rank, P<0.05). The survival probability for children with CD4 count above threshold for immunodeficiency were significantly higher than those with CD4 count below threshold at initiation of ART (log rank, P<0.05). Children on ART that had anemia at initiation of ART had lesser survival probability compared to those with no anemia (log rank, P<0.05). Children that initiated ART at advanced stage of the disease (WHO stage IV) progression had significantly lower survival probability compared to those who imitated early in the disease progression (log rank, P<0.05) (Figure 2).

Factor associated with survival rate of children living with HIV/AIDS and who started ART

In multivariable Cox regression analysis, children with Low hemoglobin level (<10 gm/dl) at ART initiation were 2.49 times (AHR=2.60, 95% CI=1.348 to 4.610, P=0.002) more likely to die as compared to those with hemoglobin level 10 gm/dl and above after adjusting for the effect of nutrition status, CD4 count, and WHO staging. Children that were presented for treatment with advanced WHO staging (stage IV) had almost three times (AHR=2.99, 95% CI=1.237 to 7.245, P=0.015) the risk of death of those presented at early staging (stage I/II). The risk of death for children with CD4 count below threshold for immunodeficiency was more than three times (AHR=3.33, 95% CI 1.401 to 7.923, P=0.004) higher than those children with CD4 count above threshold. Children with low weight for age (underweight) at ART initiation were nearly two and half times (AHR=2.42, 95% CI 1.239 to 4.744, P=0.008) more likely to die as compared to those with normal weight (Table 4).

Time in month	No of children at start	Number of deaths	Survival function
3	518	23	0.958
6	499	10	0.939
12	477	6	0.928
24	441	1	0.926
36	390	1	0.923
48	276	1	0.920
54	208	1	0.916

Table 3: Estimates of the cumulative progression to death for the cohort of children (N=560) starting ART b/n January 1, 2006 up to December 30, 2010.

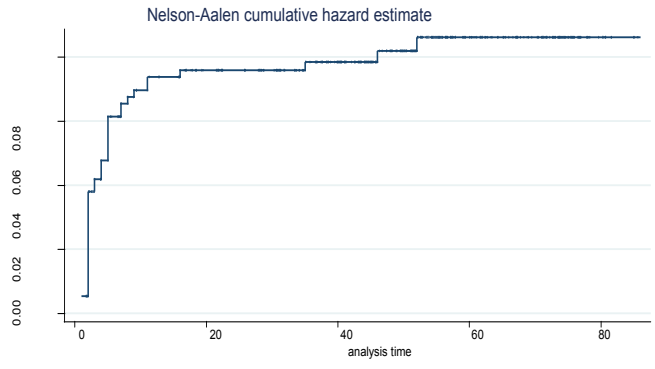

Figure 1: Nelson-Alen cumulative hazard of children on ART at Adama referral hospital and medical college, January 1st, 2006-December 30th, 2010.

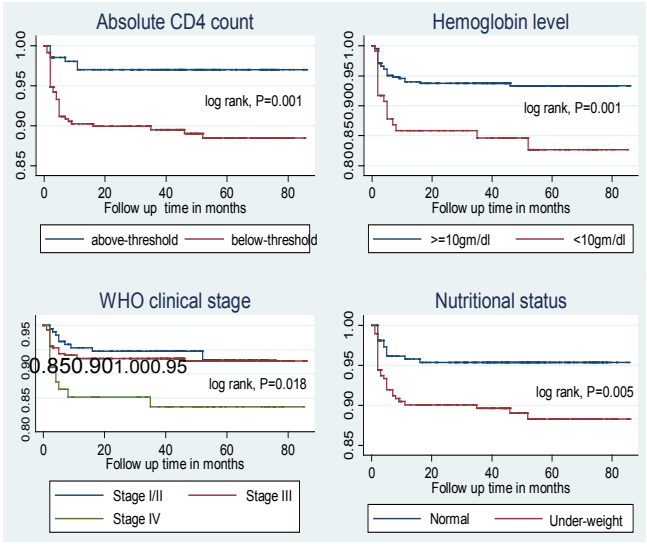

Figure 2: Survival curves for children on ART according to their nutritional status, CD4 level, Hgb level, and WHO clinical stage at initiation of ART at Adama referral hospital and Medical College, 2006-2010.

Variable	AHR (95% CI)	P values
Absolute CD4 count		
Above threshold	1	1
Below threshold	3.33 (1.401-7.923)	0.006*
Hemoglobin (n=522)		
≥ 10 gm/dl	1	1
< 10 gm/dl	2.49 (1.348-4.610)	0.004*
WHO clinical staging		
Stage I/II	1	1
Stage III	1.17 (0.543-2.558)	0.676
Stage IV	2.99 (1.237-7.245)	0.015*
Nutritional status		
Normal	1	1
Under weight	2.42 (1.239-4.744)	0.010*

Note: *p<0.05

Table 4: Multivariable Cox regression analysis of socio-demographic characteristics, clinical and immunological status among children started ART at Adama referral hospital and medical college, between January 1st, 2006 and December 30th, 2010.

Discussion

In this study high early mortality was observed. In fact nearly three fourth of the total deaths occurred during the first six months following ART initiation. And children who survived to this period were less likely to die in the succeeding follow up time. On multivariable Cox proportional hazard regression, factors affecting survival of children following ART initiation were CD4 count below threshold for immunodeficiency, underweight for age, WHO stage IV, and low hemoglobin level at ART initiation.

The results from this study showed a significant decrease in the estimated cumulative survival; especially during the first six months following ART initiation. This finding is comparable with reports from studies conducted in Sub-Saharan African countries [21-23] and in Ethiopia [17,24,25]. However, survival estimate in this study was higher

when compared to studies from Malawi [26]. This discrepancy could be explained in three ways. Firstly, the difference in study period as there are changes in treatment and care of children on ART through time given that the Malawi study was conducted 5 years ago. Secondly, the Malawi study was conducted in small sample size (n=258) as compared to this study; and this may affect the estimation. Thirdly, it may be due to the health care system changes in Ethiopia such as task shifting and delegation of HIV/AIDS services to low and middle-level health care providers. On the other hand, survival estimate in our study was lower when compared to children on ART in developed nation. Children in developed countries had higher CD4 level and lower baseline viral load at ART initiation. This generally indicates that children in resource rich countries initiate ART earlier in their illnesses which resulted in higher survival probability following ART initiation [27]. Three fourth of the total deaths in our study occurred in the first sixth months following ART initiation. This finding was similar to other studies conducted in sub-Saharan Africa [16,22,23,28] which showed 69%-89% of deaths in the first sixth months of ART initiation. This could be due to delayed presentation for treatment as it is evidenced by this study that more than two third of the children had WHO stage III/IV, more than half had CD4 count below threshold for immunodeficiency, and more than half had growth failure (underweight for age) at initiation of ART.

In our study, children with absolute CD4 count below the threshold level for immunodeficiency at initiation of ART have higher risk of death than those children with CD4 count above threshold. This finding is consistent with reports from studies conducted on cohorts of children in Africa [16,21,25,29-31]. The results from this study showed that large proportion of the children had risk factor for immune reconstitution inflammatory syndrome (IRIS) such as low weight for age and severe immune suppression [30]. Consequently, it is also possible that IRIS has a role in some of the deaths. Our result indicates that anemia as a predictor of mortality for children on ART is consistent with reports from several pediatric studies [16,23,25,32-35]. The levels of anemia in question (Hgb<10 g/dl) are modest and would not normally lead to rapid clinical deterioration [34]. However, in children living with HIV/AIDS it is a surrogate marker for advanced stage of HIV/AIDS [33]. As it is evidenced in this study, more than 70% of the children started ART at advanced WHO clinical stage.

Children with growth failure (measured as low weight-for-age) were another predictor of mortality for children on ART. This finding is consistent with reports from different pediatric studies [25,28-30,34-36]. In the context of this study, in which more than two third of children classified in immune suppressed category, low weight for age would contribute additional risk of death due to nutritional deficiency. It is plausible that children with conditions, advanced HIV/AIDS and severe malnutrition will have limited capacity for immune recovery and are susceptible to life threatening opportunistic infections. Consequently, this will increase the risk of death of children on ART. We also found advanced WHO clinical staging as another predictor of mortality for children after initiation of ART. Our finding of advanced clinical stage as predictor of mortality for children on ART was also supported by reports from other studies in Africa [21,24,25,34,35,37]. It is expected that the capacity of immune recovery will be limited for children with advanced WHO clinical stage (stage IV) at initiation of ART. And this will lead to the occurrence of life threatening opportunistic infections and increased risk of early death.

As limitation of this study Mortality might be underestimated as the considerable number of children lost to follow up may include children who died. In addition, the use of secondary data source as incompleteness was inevitable. Lack of information on the possible cause of death; over representation of older children (age above 5 years) and lack of viral load information might affect survival of children under ART treatment. Therefore any interpretation of this finding within these variables shall take into account the degree of precision. The strength of this study is the use of standard measurements which is enabled to make the comparison of findings with other national and international literatures to be valid. In addition, considering long duration of follow up period of children on ART; use of analytical study (retrospective cohort); the availability of data on important predictors of mortality (CD4 count, hemoglobin, and nutritional status); adequate sample size (strong power) were the strongest side of this study. It helps increase the quality of care given for children in ART clinic/ It gives a clue how effective care and treatment of children on ART in resource limited settings like Ethiopia. It can serve as baseline information for further study, especially on the nutritional status of children on ART.

Conclusion

The findings of this study indicate that the estimated cumulative survival was 95.8% after 3 months, 93.9% after 6 months, and 92% after 12 months of ART initiation. The cumulative survival after 54 months was 91.6% and stayed stable. Most of the children initiated ART at older age. The overall mortality rate was 2.06 deaths per 100 child-years (43 deaths over a 2078 child-years). Three fourth of the total deaths in our study occurred in the first sixth months following ART initiation. CD4 count below threshold for immune deficiency, anemia (Hgb<10 gm/dl), advanced WHO staging, and underweight were the most factors affecting survival of children following ART initiation. Based on the findings the ART services providing should engage close follow up of HIV exposed children to make early diagnosis and treatment initiation before the development of severe immune deficiency and advanced clinical stage. Targeted interventions should be prepared to intensify support and care for children especially during the first sixth months of ART initiation. Particular attention should be given to those presenting with anemia. Malnourished children should get proper care such as nutritional intervention to reduce the risk of death. Developing a mechanism to control the completeness of baseline and follow up data being collected. More over the Adama town health office and Oromia Regional Health Bureau should develop multi sectoral approach to improve the survival of children on ART and improving the capacity of health care providers through in service training.

Acknowledgement

We acknowledge the Oromia Regional Health Bureau and Mekelle University, College of Health sciences and Tulane University, USA for financial assistance. We extend our deepest gratitude to staffs of Adama referral hospital for facilitating good conditions to carry out the study. Lastly we thank the data collectors for their full commitment and technical support.

References

1. UNAIDS (2012) Report On The Global AIDS Epidemic. New York, USA 8-12.
2. UNAIDS (2011) World AIDS Day Report. New York, USA 15-18.
3. Newell ML, Coovadia H, Cortina-Borja M, Rollins N, Gaillard P, et al. (2004) Mortality of infected and uninfected infants born to HIV-infected mothers in Africa: a pooled analysis. Lancet 364: 1236-1243.
4. WHO (2011) Treatment for children with HIV.
5. KIDS-ART-LINC Collaboration (2008) Low risk of death, but substantial program attrition, in pediatric HIV treatment cohorts in Sub-Saharan Africa. J Acquir Immune Defic Syndr 49: 523-531.
6. Violari A, Cotton MF, Gibb DM, Babiker AG, Steyn J, et al. (2008) Early antiretroviral therapy and mortality among HIV-infected infants. N Engl J Med 359: 2233-2244.

7. Reddi A, Leeper SC, Grobler AC, Geddes R, France KH, et al. (2007) Preliminary outcomes of a paediatric highly active antiretroviral therapy cohort from KwaZulu-Natal, South Africa. BMC Pediatr 7: 13.

8. Rouet F, Fassinou P, Inwoley A, Anaky MF, Kouakoussui A, et al. (2006) Long-term survival and immuno-virological response of African HIV-1-infected children to highly active antiretroviral therapy regimens. AIDS 20: 2315-2319.

9. Song R, Jelagat J, Dzombo D, Mwalimu M, Mandaliya K, et al. (2007) Efficacy of highly active antiretroviral therapy in HIV-1 infected children in Kenya. Pediatrics 120: e856-861.

10. Wamalwa DC, Farquhar C, Obimbo EM, Selig S, Mbori-Ngacha DA, et al. (2007) Early response to highly active antiretroviral therapy in HIV-1-infected Kenyan children. J Acquir Immune Defic Syndr 45: 311-317.

11. Gibb DM, Duong T, Tookey PA, Sharland M, Tudor-Williams G, et al. (2003) Decline in mortality, AIDS, and hospital admissions in perinatally HIV-1 infected children in the United Kingdom and Ireland. BMJ 327: 1019.

12. Bolton-Moore C, Mubiana-Mbewe M, Cantrell RA, Chintu N, Stringer EM, et al. (2007) Clinical outcomes and CD4 cell response in children receiving antiretroviral therapy at primary health care facilities in Zambia. JAMA 298: 1888-1899.

13. World Health Organization (2010) Antiretroviral therapy for HIV infection in infants and children: Towards Universal Access. Recommendations for a public health approach, Geneva, Switzerland.

14. Federal Ministry of Health of Ethiopia (2007) Guideline for implementation of the ART programme in Ethiopia. Addis Ababa, Ethiopia.

15. Adama Referral Hospital and Medical College (2013) ART monthly report. Adama.

16. Koye DN, Ayele TA, Zeleke BM (2012) Predictors of mortality among children on Antiretroviral Therapy at a referral hospital, Northwest Ethiopia: a retrospective follow up study. BMC Pediatr 12: 161.

17. World Health Organization (2006) Antiretroviral therapy for HIV infection in adults and adolescents: recommendations for a public health approach 2006 revision. Geneva: 2006.

18. Lutter CK (2008) Iron deficiency in young children in low income countries and new approaches for its prevention, a review. J Nutr 138: 2523-2528.

19. World Health Organization (WHO) (1999) Management of severe malnutrition: a manual for physicians and other senior health workers.

20. David W Hosmer, Stanley Lemeshow (1999) Applied Survival Analysis. Regression modeling of time to event data. John Wiley & Sons. Inc, USA.

21. Edmonds A, Yotebieng M, Lusiama J, Matumona Y, Kitetele F, et al. (2011) The Effect of Highly Active Antiretroviral Therapy on the Survival of HIV Infected Children in a Resource Deprived Setting: A Cohort Study. PLoS Med 8: e1001044.

22. Zanoni BC, Phungula T, Zanoni HM, France H, Feeney ME (2011) Risk Factors Associated with Increased Mortality among HIV Infected Children Initiating Antiretroviral Therapy (ART) in South Africa. PLoS ONE 6: e22706.

23. Bolton-Moore C, Mubiana-Mbewe M, Cantrell J, Chintu N, Stringer EM, et al. (2007) Clinical outcomes and CD4 response in children receiving antiretroviral therapy at primary health care facilities in Zambia. JAMA 298: 1888-1899.

24. Workneh N, Girma T, Woldie M (2009) Immunologic and clinical outcomes of children on HAART: A retrospective cohort analysis at Jimma University Specialized Hospital. Ethiop J Health Sci 19: 75-82.

25. Taye B, Shiferaw S, Enquselassie F (2010) The impact of malnutrition in survival of HIV infected children after initiation of antiretroviral treatment (ART). Ethiop Med J 48: 1-10.

26. Fertzer BC, Heissenipour MC, Kamthuzi P, Hyde L, Bramson B, et al. (2009) Predictors for mortality and loss to follow-up among children receiving anti-retroviral therapy in Lilongwe, Malawi. Trop Med Int Health 14: 862-869.

27. Peacock-Villada E, Richardson B, John-Stewart G (2009) Paediatric HAART treatment outcomes: A comparison of developing and developed countries. 16th Conference on Retroviruses and Opportunistic Infections CROI 2009), Montreal, Canada.

28. Lambiganon P, Kariminia A, Aurpibul L, Hansudewechakul R, Puthanakit T, et al. (2011) Survival of HIV-infected children: A cohort study from the Asia Pacific region. J Acquir Immune Defic Syndr 56: 365-371.

29. Collins IJ, Jourdain G, Hansudewachakul R, Kanjanavanit S, Hongsiriwon S, et al. (2010) Long-Term Survival of HIV-Infected Children Receiving Antiretroviral Therapy in Thailand: A 5-Year Observational Cohort Study. Clin Infect Dis 65: 414-421.

30. Smith K, Kuhn L, Coovadia A, Meyers T, Hu CC, et al. (2009) Immune reconstitution inflammatory syndrome among HIV-infected South African infants initiating antiretroviral therapy. AIDS 23: 1097-1107.

31. Fenner L, Brinkhof MW, Keiser O, Weigel R, Cornell M, et al. (2010) Early Mortality and Loss to Follow-up in HIV-Infected Children starting Antiretroviral Therapy in Southern Africa. J Acquir Immune Defic Syndr 54: 524-532.

32. Isaakidis P, Raguenaud ME, Te V, Tray CS, Akao K, et al. (2010) High survival and treatment success sustained after two and three years of first-line ART for children in Cambodia. J Int AIDS Soc 13: 11.

33. Janssen N, Ndirangu J, Newell ML, Bland RM (2010) Successful pediatrics HIV treatment in rural Africa. Arch Dis Child 95: 414-421.

34. Wamalwa DC, Obimbo EM, Farquhar C, Richardson BA, Mbori-Ngacha DA, et al. (2010) Predictors of mortality in HIV-1 infected children on antiretroviral therapy in Kenya: a prospective Cohort. BMC Pediatr 10: 33.

35. Anaky MF, Duvignac J, Wemin L, Kouakoussui A, Karcher S, et al. (2010) Scaling up antiretroviral therapy for HIV-infected children in Côte d'Ivoire: determinants of survival and loss to programme. Bull World Health Organ 88: 490-499.

36. Sutcliffe CG, van Dijk JH, Munsanje B, Hamangaba F, Sinywimaanzi P, et al. (2011) Weight and height z-scores improve after initiating ART among HIV-infected children in rural Zambia: a cohort study. BMC Infect Dis 11: 54.

37. Bong CN, Yu JK, Chiang HC, Huang WL, Hsieh TC, et al. (2007) Risk factors for early mortality in children on adult fixed-dose combination antiretroviral therapy in a central hospital in Malawi. AIDS 21: 1805-1818.