Original article

Factors affecting the survival of HIV-infected children after ART initiation in Bahir-Dar, Ethiopia

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Abstract

Background: The attention given to HIV-infected children in terms of providing ART had so far taken a second rank. This was because primary concern is about adults.

Objectives: This study had the objectives to estimate the survival duration and identify socio-economic, demographic and clinical predictor variables that affect the survival of HIV-infected children under ART.

Methods: The data used in this study were obtained from the medical records of 255 HIV-infected children under the age of 15 who received ART in Felege-Hiwot Referral Hospital, Ethiopia. The Kaplan-Meier method and log-rank test allowed for comparison of survival of patients in different categories. Identification of predictors of survival was accomplished by employing the Cox proportional hazards regression model.

Results: The mean survival time was found to be 22.4 months with standard deviation of 0.7 months. Baseline hemoglobin level, WHO clinical stage and age had significant impact on the survival of children during the 30 months of follow up.

Conclusion: The risk of death among HIV-infected children with lower hemoglobin level in younger age groups was higher compared to those who were older and had higher hemoglobin level; the risk was highest in stage IV which was very similar to that in stage III. [*Ethiop. J. Health Dev.* 2012;26(3):193-199]

Introduction

The HIV pandemic has created unprecedented burden on the economies and health care systems of countries, particularly in Sub-Saharan Africa, where the prevalence is highest. The total number of children under 15 years of age living with HIV/AIDS in 2008 worldwide was reported as 2.1 million including 430,000 newly infected, of whom 390,000 new cases were in sub-Saharan Africa (1). In 2010 an estimated 1,216,908 people were living with HIV/AIDS of whom 79,871 were children. It was estimated that 397,818 HIV-positive cases were in need of antiretroviral treatment (ART) out of whom 26,053 (6.5%) were children under 15 years of age. It was also estimated that the adult (15 to 49 years of age) HIV prevalence in Amhara Region, Ethiopia, in 2010 was 2.9% with 155,694 males and 223,372 females; the number of HIV positive children in the region was expected to increase due to mother-to-child transmission at birth and/or during breast-feeding (2).

Recognizing the urgent need for ART, the government of Ethiopia issued the first antiretroviral guideline in 2003, which was the same year that the treatment began. Comprehensive care and support for HIV-infected children should be provided in a care-and-treatment center, preferably where the patients receive treatment. Close regular follow-up is important since these children are at risk of morbidity and mortality. Mortality estimates in Africa show that without treatment 35.2% of HIV-infected children die in their first year and 52.5% by age two. This underscores the importance of timely antiretroviral treatment-care and -support (3).

In resource-rich settings HAART had changed the face of pediatric HIV. HIV-infected children now survive to adolescence and adulthood. However, the experience in pediatric HIV/AIDS care and treatment in Ethiopia is limited. Major obstacles to scaling-up pediatric care include: lack of human resources and scarcity of pediatric service providers, no systematic effort to identify and follow HIV exposed infants, limited availability of virologic testing, lack of provider-initiated HIV testing, missed opportunity for testing children, insufficient advocacy and understanding that ART is efficacious in children, and limited experience with program implementation to provide pediatric HIV/AIDS care and treatment. Consequently too few children start ART in Ethiopia (3).

It is not a hidden fact that the HIV/AIDS pandemic is a serious burden on the economic, social and political issues of the world in general, and in developing countries in particular. These days countries provide ART drugs to people who are living with HIV/AIDS, in order to decrease infection from opportunistic diseases, reduce HIV/AIDS-related deaths and to improve quality of life to those infected with HIV.

The use of highly active antiretroviral therapy (HAART) has resulted in a significant decline in AIDS-related deaths and complications among adults and adolescents. However, the medical management of HIV-infected children remains challenging. Access to HIV treatment is limited and early treatment initiation can cause serious complications. Since there is currently no cure for HIV, a balance between treating the disease and maintaining quality of life must be weighed carefully. An evaluation

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to determine an appropriate time to initiate HAART is necessary to improve both the quality of life and survival of HIV-infected children (4).

The introduction of ART presented an enormous opportunity in terms of reducing morbidity and mortality due to AIDS worldwide. Ethiopia has been engaged in the scale-up of ART access to its people since 2005. The free ART program was launched in July 2005. The service was expanded from only three health facilities in 2005 to 400 in 2008. The number of people who started ART has also shown an unprecedented increase during the same period from 900 in 2005 to 180,447 by the end of December 2008 (5).

In 2009, a single point estimate of AIDS related deaths for 2010 was 44,751 of whom 7,214 were children and there were about 84,189 HIV positive pregnancies from which 14,140 led to the birth of HIV-positive children and this resulted in an estimated increase in the number of HIV positive children from 72,945 in 2009 to 79,871 in 2010 (2).

The total number of HIV-positive people in Ethiopia was estimated to be 1,326,329 including 137,494 new infections and excluding the 28,073 AIDS related deaths in 2010. It is also estimated that there were a total of 90,610 HIV-positive children under 15 years of age including 14,276 new infections and excluding 3,537 AIDS related deaths of children that occurred during the year (6).

According to the Federal HIV/AIDS Prevention and Control Office, the single point estimate for prevalence of HIV/AIDS among adults for 2007 was estimated at 2.1% of whom 7.7% and 0.9% were living in urban and rural areas (3). In 2010, the FHAPCO estimated overall adult HIV prevalence at 2.4%. Urban and rural HIV prevalence rates were 7.7% and 0.9%, respectively. In 2010, an estimated 28,073 Ethiopians died of AIDS increasing the number of children who have lost one or both parents because of AIDS to 804,184 (6).

HIV/AIDS has been and still is the greatest challenge to the Ethiopian health system, as elsewhere in sub-Saharan African countries. It has remained to be among the major causes of deaths over the past two decades. An estimated one million people were living with HIV in Ethiopia of whom nearly 397, 818 needed antiretroviral care and treatment (7).

This study was based on data about HIV-infected children (in the age bracket from 1 to 15 years) who started ART in Felege-Hiwot Referral Hospital in Bahir-Dar, the capital of the Amhara Regional State, Ethiopia. Bahir-Dar is located some 560 km north-west of Addis Ababa. The city is one of those cities in Ethiopia where HIV prevalence is high according to the National Factsheet, 2010. At this juncture it is worthwhile pointing out that a longitudinal study on adults who received ART in the hospital was undertaken by Bayeh et al. (2010).

The objectives of this research were (i) to estimate the survival, and (ii) to identify socio-economic, demographic and clinical predictor variables that affect HIV-infected children taking ART. It is hoped that the study will provide information that would fill the existing knowledge gap about children under ART.

Methods

***Data*:**

This study used secondary data on children who had enrolled in the pediatric ART unit from 2007 to early 2009. Since 2005 Felege-Hiwot Referral Hospital has been providing care to HIV-infected adults and children through the government free ART program with additional support from the nongovernmental organization I-TECH Ethiopia. The ART unit had physicians, nurses, counselors and laboratory technicians working full time.

The data for the study were obtained from follow up records of HIV-patient children database. The data about children were filtered from the database. No contact was made with any child so as to maintain privacy and confidentiality. The database included demographic, laboratory and clinical data of HIV-infected children who were being followed up for 30 months in the years 2007 to 2009. The total number of children on ART was more than 819. Since only 255 patients had full records, this study was based on the data of those children with complete history. It is a known fact that in an observational study like this there is little or no control on the sample size of subjects (in this case HIV-infected) patients; in that sense a study based on the present sample did enable us to achieve the objectives set.

It is worthwhile pointing out that, in lieu of keeping a reasonable number of predictors (in relation to the sample size) in the model, interactions among the main factors were not considered. Hence, the study was based on a main-effects model.

The response variable in this study was “survival time” of HIV-infected children after starting ART. The survival time was measured as the length of time in months a child had been followed up from the time a child started ART until death or the child was lost to follow up and was still on follow up.

The predictor variables considered in this study were those that were likely to affect survival status. Even though it was desirable to include as many socio-economic, demographic, clinical and virological, and other variables the study was based on those that were included in the records of the ART unit. The predictors considered in this study were: four continuous covariates (age, hemoglobin, weight, CD4) and seven categorical variables (gender, prophylaxis, TB-treatment status, reason for starting ART, functional status, WHO clinical stage, type of ART drug). Functional status was included because in the context of a poor economic condition,

children were forced to work in early life, especially in rural settings.

***Data Analysis*:**
This study employed two standard statistical methods: a non-parametric method called Kaplan-Meier method and the associated log-rank test (8), and a semi-parametric method known as Cox-proportional hazards regression model (9). For the theory and applications of these methods the interested reader can consult, among other sources, (10-12).

Results
General:
Data on a total of 255 HIV infected children who started ART at Felege-Hiwot Referral Hospital in Bahir-Dar from 2007 up to early 2009 were used. From among these children 71 (27.84%) died due to the disease, 19 (7.45%) were lost to follow up while 165 (64.71%) were still alive. We note that the number of censored observations was 184 which is about 72.2% of the total; this is a high proportion. A consequence of this was that the mean survival time was slightly underestimated. The mean survival was found to be 22.4 months with standard deviation of 0.7 months.

A description and the associated distribution of 11 socio-economic and clinical predictor variables upon which the analysis in this study was based are given in Table 1. The four continuous covariates age, hemoglobin, weight and CD4 count were categorized into clinically meaningful groups so that it would be easy to describe and interpret the results.

Table 1: **Socio-demographic and clinical characteristics, Felege-Hiwot Hospital, Bahir-Dar, 2007-2009 (*n* =255).**

Variable/factor	Category	Total	Dead	Censored	Percent
Gender	Male	141	38	103	73.0%
	Female	114	33	81	71.1%
Prophylaxis taken	No	103	26	77	74.8%
	Yes	152	45	107	70.4%
TB treatment started	No	204	58	146	71.6%
	Yes	51	13	38	74.5%
Reason for staring ART	CD4 and Clinical reasons	155	47	108	69.7%
	CD4 only	69	16	53	76.8%
	Clinical only	31	8	23	74.2%
Functional Status	Working	165	42	123	74.5%
	Ambulatory	66	20	46	69.7%
	Bedridden	24	9	15	62.5%
WHO Clinical Stage	Clinical Stage-I	23	5	18	78.3%
	Clinical Stage-II	49	8	41	83.7%
	Clinical Stage-III	122	28	94	77.0%
	Clinical Stage-IV	61	30	31	50.8%
	d4t-3TC-NVP	64	17	47	73.4%
	d4t-3TC-EFV	32	9	23	71.9%
Type of ART drug	AZT-3TC-NVP	100	30	70	70.0%
	AZT-3TC-EFV	59	15	44	74.6%
	[1-1.5) Years	29	14	15	51.7%
Age	[1.5-5) Years	89	27	62	69.7%
	[5-15) Years	137	30	107	78.1%
	≤7g/dl	93	44	49	52.7%
	(7-8.5]g/dl	36	13	23	63.9%
Hemoglobin	(8.5-10)g/dl	37	7	30	81.1%
	10g/dl and higher	89	7	82	92.1%
	Above threshold	98	27	71	72.4%
CD4 count	Below threshold	157	44	113	72.0%
	Normal body weight	149	49	100	67.1%
Weight	Low body weight	52	12	40	76.9%
	Very low body weight	54	10	44	81.5%

Note: The last four continuous variables at the bottom have been divided into categories thereby allowing the use of log-rank test procedure.

***Results of the Descriptive Analysis*:**
For the categorical covariates, the analysis included Kaplan-Meier estimates of the group specific survivorship functions, point and interval estimates of the mean survival time and log-rank significance tests. These were used to compare survival time across the groups defined by the predictor variable. Note that the continuous covariates are treated as categorical based on the grouping scheme explained earlier. Though not included here (in the interest of not making the paper lengthy), graphs of estimated Kaplan-Meier survival functions were used in the analysis so as to provide visual impression on the survival experience of different groups of the study subjects. The findings (both numerical and graphic) testified that the survival time of HIV-infected children after initiation of ART was

associated with the predictor variables hemoglobin level, WHO clinical stage, age, weight and functional status.

In addition to the descriptive results that were based on the Kaplan-Meier estimates, the log-rank test was performed to find out any possible significant differences in survival experience between/among various levels of the categorical variables as well as the categorized continuous variables (Table 2). The p-values showed that there were no statistically significant differences among the categories of: gender, prophylaxis, TB-treatment status, reason for starting ART, functional status, type of ART drug, CD4 group. On the other hand, the results manifested significant differences in survival among the different categories of WHO clinical stage, age and hemoglobin.

Table 2: **Log-rank test results, Felege-Hiwot Hospital, Bahir-Dar, 2007-2009 (*n* =255).**

Variable/factor	Chi-square	d.f.	*p*-value
Gender	.134	1	.714
Prophylaxis taken	.341	1	.559
TB treatment started	.355	1	.551
Reason for staring ART	1.367	2	.505
Functional Status	3.271	2	.195‘
WHO Clinical Stage	23.358	3	.000
Type of ART drug	1.342	3	.719
Age	13.238	2	.001
Hemoglobin	48.689	3	.000
CD4	.324	1	.569
Weight	4.996	2	.082

***Results of the Proportional Hazards Cox Regression Model*:**

The Cox proportional regression model with the three predictors namely, hemoglobin, WHO clinical stage and age was found to provide an appropriate means, showing that these predictors had significant impact on the survival longevity of the HIV-patient children considered in this study. The results given below are derived from the estimates in Table 3.

Table 3: **Estimates of the Cox Proportional hazards regression model, Felege-Hiwot Referral Hospital, Bahir-Dar, 2007-2009 (*n* =255).**

Variable/factor	Parameter Estimates	S.E.	Wald	d.f.	*p*-value	Est. HR	95% CI for HR	
							Lower	Upper
Hemoglobin			47.375	3	.000			
Hemgrp I	-.789	.340	5.374	1	.020	.454	.233	.885
Hemgrp II	-1.570	.415	14.296	1	.000	.208	.092	.469
Hemgrp III	-2.627	.420	39.188	1	.000	.072	.032	.165
Clinical Stage			28.237	3	.000			
Stage I	-2.022	.506	15.977	1	.000	.132	.049	.357
Stage II	-1.738	.272	16.875	1	.000	.176	.077	.403
Stage III	-.706	.423	6.715	1	.010	.494	.290	.842
Age			23.658	2	.000			
Age group I	-1.257	.349	12.959	1	.000	.285	.144	.564
Age Group II	-1.693	.349	23.562	1	.000	.184	.093	.365

WHO Clinical Stage: WHO clinical stage-IV was taken as the referent category for comparison of mortality with mortality in the remaining three categories. The estimated hazard ratio (HR) for WHO clinical stage III was 0.494 (with 95% CI: 0.290-0.842). This means 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). The estimated HR for WHO clinical stage II was 0.176 (with 95% CI: 0.077-0.403). Children with baseline WHO clinical stage II were 82.4% less likely to die compared with children in the referent category. The estimated HR for WHO clinical stage I is 0.132 (with 95% CI: 0.049-0.357). Children with baseline WHO clinical stage I were 86.8% less likely to die compared with children in the referent category.

Hemoglobin Level: Here hemoglobin group 0 (with values less than or equal to 7g/dl) was taken as the referent category. The estimated HR for the hemoglobin group I ([8.5g/dl - 10.0g/dl)) was 0.454 (with 95% CI: 0.233-0.885). The implication is that children belonging to hemoglobin group I were 54.6% less likely to die compared with children in the referent category. The estimated HR for the hemoglobin group II ([8.5g/dl - 10.0g/dl)) was 0.208 (with 95% CI: 0.092-0.469). Children belonging to hemoglobin group II were 79.2% less likely to die compared with children in the referent category. The estimated HR for the hemoglobin group III

(10g/dl and more) was 0.072 (with 95% CI: 0.032-0.165). Children with the latter hemoglobin level were 92.8.8% less likely to die compared with children in the referent category.

Age: The referent age category here was age group 1 to below 1.5 (exclusive) years. The estimated HR for age group I, that is 1.5 to just under 5 years, was 0.285 (with 95% CI: 0.144-0.564) implying that at any time during the study period, children in this age bracket were 71.5% less likely to die compared with children in the referent category. The estimated HR for age group II, that is 5 to nearly 15 years, was 0.184 (with 95% CI: 0.093-0.365). The children in this age group were 81.6% less likely to die compared with children in the referent category.

Discussion

Similar studies have shown that the survival of HIV-infected patients after initiation of ART was a function of baseline variables like CD4 count, clinical stage of the disease, weight, age, drug adherence, types of treatment (mono-therapy, bi-therapy or triple-therapy), viral load, nutrition, hemoglobin level and others.

We discus here some relevant results from previous research undertakings that were made on the problem area in relation to the issue that this study addressed. The discussion is relevant because the research works, with the exception of one, had been done in developing countries where there are comparable similarities in resource settings and limitations.

A study based on 255 HIV-positive children treated with first-line ART for at least 24 months was made to identify risk factors associated with treatment failure in Cambodia (13). The results showed that ART had the desired effect in improving the survival of children, raise CD4 count, suppress viral load and led to weight increment among children with viral load below 1000 copies/ml. In the case of children with viral load above 1000 copies/ml only CD4 count and CD4 percentages below the threshold attributed to severe immunologic suppression showing treatment failure. However, orphan status and caregiver characteristics such as literacy, age and socio-economic status were not associated with treatment failure after 24 months of ART.

In a study to evaluate changes and risk factors for death among HIV-infected children in pediatric AIDS clinical trials in the US, 3,553 HIV-infected children were followed up for a median of 5.3 years. The study showed that increased risk of death was significantly associated with low CD4, pneumonia and AIDS-defining illness at entry, whereas decreased risks of mortality were identified for children who began HAART timely (14).

A retrospective cohort study was undertaken to assess clinical factors associated with growth in HIV-infected children on ART in Uganda. Height and weight measurements on 749 children included in the study were taken before ART initiation and for at least six months after ART initiation. Descriptive and logistic regression analyses were conducted to identify covariates associated with the risk of either stunting or being underweight. It was found that children in WHO clinical-stages II, III, and IV at baseline were 1.5 times more likely to become underweight as compared to children in clinical stage I; initiation of ART resulted in improvement in mean standardized weight-for-age. Weight-for-age z-score improved significantly after initiation of ART. This pediatric population gained weight more rapidly than height after initiation of ART (15).

A study conducted in nine African countries and Brazil to evaluate the prognostic effect of selected laboratory and growth markers about short-term risk of mortality on HIV-infected children who did not receive ART showed that, CD4 percentage and CD4 cell count were the strongest predictors of mortality, followed by weight-for-age and hemoglobin level (16).

The impact of daily co-trimoxazole prophylaxis and ART on HIV-infected Zambian children using randomized control trial was studied. The results showed that mortality rate was high among children who had low current weight-for-age, leading to the conclusion that low weight-for-age score is a predicator of death (17).

The clinical, immunological, and virological effects of HAART were investigated based on HIV-infected children in Mombasa, Kenya. The results revealed that weight-for-age and CD4 cell count increased as a result of the treatment while viral load decreased from the baseline figures by a factor more than 17 times (18).

The clinical and immunological outcomes on HIV-infected children enrolled in a pediatric treatment program who started ART at primary care clinics in Lusaka, Zambia were studied. It was found out that mortality rate was significantly associated with: CD4 cell depletion, lower weight-for-age, younger age, and anemia. The mean CD4 cell percentage at ART initiation for more than 53% of children, who had at least one repeat measurement, showed an increasing trend as measured every six months after initiation of ART (19).

A study on HIV-infected children under ART in Port-au-Prince, Haiti investigated the outcome of pediatric ART using retrospective data. The results showed that age below 18 months, CD4 T cell percentage and weight-for-age z-score were significant baseline predictors of child mortality (20).

A case control study was undertaken to see body composition in relation to disease progression and survival among 86 HIV-infected and 113 HIV uninfected children (control group). Weight among the HIV-infected children was significantly lower than in the control group (with similar ages), and lower weight was significantly associated with increased risk of death, leading to the conclusion that body weight-for-age is a good prognostic indicator of mortality (21).

The risk of death among HIV-infected infants and children in Cape Town, South Africa was found to be significantly associated with age below 6 months as well as the severity of the disease at time of diagnosis. Infants diagnosed before 6 months of age had significantly shorter median survival (10 months) compared with 36 months for those diagnosed at 7-12 months of age. For children over the age of 12 months the cumulative proportion survival time of 48 months was 78%. The median survival of the children considered in this study was 32 months. Children with severe disease (category C) had a median survival of 21 months, significantly lower than these in category B (32 months). For the children in category A the cumulative proportion survival time of 48 months was 66% (22).

The above sources showed that the most significant predictors of survival longevity were: CD4 count advanced WHO clinical stages, age, weight and to some extent opportunistic diseases like anemia and pneumonia. The findings of the current study identified WHO clinical stage, age and hemoglobin level as determinant predictors of survival of HIV-infected children who were receiving treatment at Felege-Hiwot Referral Hospital. Weight did not come out as a strong predictor although it is a clinically meaningful determining variable. In spite of that, the conclusions reached here are mostly in agreement with those in the studies discussed above.

In conclusion, the findings of this study showed that the risk of death among HIV-infected children with lower hemoglobin level in younger age groups was higher compared to older children and with higher hemoglobin level; the risk was highest in stage IV which was very similar to that in stage III. As a consequence, the study recommends that ART should be initiated irrespective of age or level of hemoglobin. However, as those children with lower hemoglobin and younger age were the most vulnerable such a group of patients deserve special care and attention.

Admittedly the generality of the results of the current study have a limitation in that, from a total of 819 children on ART, complete data could be obtained for 255 patients. This is a natural consequence of an observational study like this one, and therefore, the researcher has little or no control on the sample size of subjects under consideration.

As prevention of mother-to-infant transmission has not been practiced before or at the time when the patient children included in this study were born, we could attribute the high rate of death among the very young children partly to the absence of a program geared to transmission of the virus to a child.

We also recommend that similar studies need to be undertaken by including relevant socio-economic, demographic, behavioral and clinical covariates that have not been captured in the database at Felege-Hiwot Referral Hospital. Such a consideration would widen the horizon of knowledge in the problem area that this study has attempted to address.

References

1. Joint United Nations Program on HIV/AIDS (UNAIDS) and World Health Organization (WHO) 2009, AIDS Epidemic Update, Geneva, 2009.
2. National AIDS Resource Center 2009, Website [cited 2012]; Available from: URL: http://www.etharc.org/resources/healthstat/nationalfactsheet/12-nationalfactsheet2009.
3. Federal Ministry of Health. Guidelines for pediatric HIV/AIDS care and treatment in Ethiopia: FHAPCO; Addis Ababa, 2007.
4. National Institute of Allergy and Infectious Diseases (NIAID) [cited 2012]; Available from: URL: http://clinicaltrials.gov/ct2/show/ NCT00234091
5. Seyoum E, Mekonen Y, Kassa A, Eltom A, Damtew T, Lera M, Felema B, Assefa Y. ART scale-up in Ethiopia: Success and challenges: HAPCO Plan, Monitoring and Evaluation Directorate 2009; Addis Ababa, Ethiopia.
6. National Factsheet 2010, Website [cited 2012]; Available from: URL;http://www.etharc.org/resources/healthstat/nationalfactsheet/13-nationalfactsheet2010.
7. Bayeh Abera, Fisseha Walle, Tsehaye Tewabe, Atnaf Alem, Mohammed Yessin. ART-naïve HIV patients at Felege-Hiwot Referral Hospital, Northwest Ethiopia. *Ethiop J Health Dev* 2010;24(1):3-8.
8. Kaplan EL, Meier P. Nonparametric estimation from incomplete observations. *Journal of the American Statistical Association* 1958;53:457-481.
9. Cox DR. Regression models and life tables (with discussion). *Journal of the Royal Statistical Society* 1972; Series B, 34:187-220.
10. Collet D. Modelling survival data in medical research, 2nd Ed. Chapman & Hall/CRC; London, 2003.
11. Hosmer DW, Lemeshow S, May S. Applied survival analysis, 2nd Ed. John Wiley & Sons, Inc.; New York, 2008.
12. Lawless JF. Statistical models and methods for lifetime data, 2nd Ed. John Wiley & Sons, Inc.; New York, 2003.
13. Petros I, Raguenaud M, Te V, Tray CS, Akao K, Kumar V, Ngin S, Nerrienet E, Zachariah R. High survival and treatment success sustained after two and three years of first-line ART for children in Cambodia. *J Int AIDS Soc* 2010;13:11-20.
14. Brady MT, Oleske JM, Williams PL, Elgie C, Mofenson LM, Dankner WM, Van Dyke RB. Declines in mortality rates and changes in causes of death in HIV-1-infected children during the HAART era. *J Acquir Immune Defic Syndr* 2010;53(1):86-94.
15. Kabue MM, Kekitiinwa A, Maganda A, Risser JM, Chan W, Kline MW. Growth in HIV-infected children receiving antiretroviral therapy at a

pediatric infectious diseases clinic in Uganda. *AIDS Patient Care STDS* 2008;22(3):245-51.

16. Gibb DM, Duong T, Dunn D, Chintu C, Mulenga V, Cotton M, et al. Markers for predicting mortality in untreated HIV-infected children in resource-limited settings. *AIDS* 2008;22(1):97-105.
17. Walker SA, Mulenga V, Ford D. The impact of daily cotrimoxazole prophylaxis and antiretroviral therapy: Mortality and hospital admission in HIV-infected Zambian children. *Am J Clin infect Dis* 2007;44:1361-1367.
18. Song RJ. Efficacy of highly active antiretroviral therapy in HIV-1-infected children in Kenya. *Pediatrics* 2007;120(4):856–861.
19. Bolton-Moore M. Clinical outcomes and CD4 cell response in children receiving antiretroviral therapy at primary health care facilities in Zambia. *Journal of the American Medical Association* 2007;298(16): 1888-1899.
20. George E, Noel F, Bois G. Antiretroviral therapy for HIV-1- infected children in Haiti. *J Infect Dis* 2007;195:1411-1418.
21. Fontana M, Zuin G, Plebani A. Body composition in HIV infected children: Relations with disease progression and survival. *Am J Clin Nutr* 1999;69:1282-86.
22. Hussey GD, Reijnhart RM, Sebens AM, Burgess J, Schaaf S, Potgieter S. Survival of children in Cape Town known to be vertically infected with HIV-1. *S Afr Med J* 1998;88(5):554-8.