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Attrition and loss to follow-up Among Children and Adolescents in a Community Home-Based Care HIV Programme in Uganda

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Abstract

Background: We examine attrition and loss to follow-up (LTFU) and their baseline predictors among HIV-infected children and adolescents in a Community Home-Based Care (CHBC) model in Kampala (Uganda).

Methods: We conducted a retrospective cohort analysis of attrition and LTFU and their predictors among children and adolescents aged 0-20 years in the Tukula Fenna project. The project operates at the Home Care Department of Nsambya Hospital and four outreach clinics, located in Kampala and three surrounding districts in Uganda. The project uses community home-based care to provide free Antiretroviral Therapy (ART), other medical treatment as necessary, nutritional support, psychosocial support, and home visits. Kaplan-Meier curves were used to assess attrition and LTFU, and multivariate Cox proportional hazard regression models were used to identify their predictors.

Results: 1162 children and adolescents with confirmed positive HIV status were enrolled in the Tukula Fenna project between October 2003 and August 2012. Over this period, 5.34% (62) of patients died 37.61% were LTFU (437), and overall attrition was 42.94% (499). This resulted in overall incidence of death of 18 per 1000 person-years, of LTFU of 126 per 1000 person-years, and of attrition of 144 per 1000 person-years. The single factor significantly associated with overall attrition among the 1162 patients was absence of ART (HR: 0.11, 95% CI: 0.09,0.14). Both baseline BMI z-score (HR: 0.96, 95% CI: 0.91, 1.00) and receipt of ART (HR: 0.12, 95% CI: 0.10, 0.15) were significantly negatively associated with LTFU among all 1162 patients in this cohort.

Conclusion: Not receiving ART was the single factor significantly associated with overall attrition. Both baseline BMI z-scores and receipt of ART were protective against LTFU among HIV positive children and adolescents enrolled in the Tukula Fenna project. Orphans need more nutritional support and improved access to early ART initiation.

Keywords: Attrition; LTFU; Retention; Children; Adolescents; CHBC; Nsambya; Uganda

Introduction

The availabilty and rapid scaling up of Antiretroviral Therapy (ART) programmes for infants and children with Human Immunodeficiency Virus (HIV) infection in Low-Middle Income Countries (LMIC) has enabled many to survive and grow into adolescents and adults [1-3]. However, retention in care of children and adolescents with HIV remains a major operational challenge requiring innovation and creativity [4-6]. Particularly, challenges associated with data collection systems may influence reporting of important outcomes such as attrition and loss to follow-up (LTFU) in these settings.

Various approaches have been employed to improve retention in HIV programmes in LMIC with varying degrees of success [7-9]. A number of studies have documented improved retention in care as well as better clinical outcomes using community-based or Community Home-Base Care (CHBC) models in Malawi, Haiti and elsewhere [10-14]. In general, CHBC includes any form of care (physical, psychosocial, palliative and spiritual) given to the sick and the affected in their own homes and care extended from the hospital or health facility to their homes through family participation and community involvement [15,16]. Home delivery of HIV counselling and testing, defaulter tracking, adherence counselling and monitoring in the home have also been shown to be associated with improved retention in care [8,17]. Other studies have demonstrated positive impacts of psychosocial support services on retention in HIV programmes in LMIC [18,19].

Thus, home delivery of basic HIV services, community-based or CHBC approaches seem to improve retention in care. However, the majority of the studies cited above were conducted in adults, and little is known about retention of children and adolescents from such approaches in LMIC. In this paper, we examine attrition and LTFU and their baseline predictors among children and adolescents in the Nsambya CHBC HIV service delivery model in Kampala, Uganda.

Methods

Study design

This retrospective cohort study utilized data routinely collected from the Tukula Fenna project between October 2003 and August 2012.

Study setting

According to the United Nations Children's Fund, by 2010, AIDS orphans accounted for 39% of all children orphaned in Uganda [20]. Approximately half of the patients in the Tukula Fenna project are orphans and recipients of Orphans and Vulnerable Children's (OVC) support. The Tukula Fenna project operates at the Home Care

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Department of St. Raphael of St. Francis Hospital (Nsambya Hospital) and four outreach clinics, located in Kampala and three surrounding districts in Uganda. Nsambya Hospital is a tertiary referral hospital in the Nsambya area of Kampala. Although Nsambya Hospital is a private-not-for-profit facility, all paediatric HIV services are free of charge due to external support from international partners (House for Life, Father Angelo, Paediatric European Network for Treatment of AIDS Foundation and the US President's Emergency Plan For AIDS Relief) and local support from the Ugandan Ministry of Health.

The Tukula Fenna project started in 2003 and provides standard and comprehensive HIV services for infants, children and adolescents within the framework of the Nsambya CHBC model. The components of the Nsambya CHBC framework include monthly on-site appointments either at the Home Care Department or at the four outreach clinics added to decentralize Voluntary Counselling and Testing (VCT), ART refills and Prevention of Mother-To-Child Transmission (PMTCT) and Early Infant Diagnosis (EID) services. Other components include a nutritional support clinic, home visits, psychosocial support workshops and services provided by a multidisciplinary outreach team (counsellors, social workers, nurses and sometimes clinicians) and an adolescents' transition clinic to prepare adolescents and their caregivers for a smooth transition to adults' HIV care. The outreach team also works with community volunteers and community leaders to identify OVC for support, as well as sensitize and mobilize communities to access HIV services.

Study population

The study included all infants, children and adolescents aged 0-20 years enrolled in the Tukula Fenna project between October 2003 and August 2012 with confirmed HIV infection and with a valid enrollment date.

Pre-ART care package

Patients were enrolled into care after VCT either at the Home Care Department or at the outreach clinics or as referrals from various sources, such as other hospitals or centres, community HIV testing sites, and self-referrals. Infants and children less than 18 months of age known or suspected to be HIV-exposed were diagnosed through HIV-1 DNA polymerase chain reaction test. Other services included cotrimoxazole prophylaxis, multivitamins supplements, screening for tuberculosis (TB), and Isoniazid Preventive Therapy (IPT) as prophylaxis and treatment for latent TB, and treatment of opportunistic infections. Laboratory evaluation involved 6-monthly CD4 cell counts and percentages and full blood counts and other tests as necessary. Nutritional status was assessed through monthly age-appropriate anthropometric measurements (weight, height and mid upper arm circumference) taken and recorded by attending nurses or nutritionists at the nutritional support clinic.

In terms of psychosocial support, paediatric patients and their care givers received various forms of counselling and social services, including monthly food incentives, free medical services, and sponsorships for basic and vocational education for some orphans and vulnerable children. Other forms of psychosocial support included children and adolescents' peer- support groups and quarterly psychosocial support workshops for paediatric patients and their caregivers. Peer-support groups consisted of 5-10 children or adolescent peers carefully selected to form a group. The group provided an atmosphere of belonging which enabled children and adolescents to share life experiences related to being HIV positive, including peer-counselling on adherence to clinical appointments and medications. In addition, drama performances by some of the adolescents in the project were used to further educate and sensitize paediatric patients on HIV prevention, positive living and other themes from time to time.

The quarterly psychosocial support workshops provided opportunities for further interactions between health care providers and paediatric patients and their caregivers outside the traditional health facilities. Discussion topics commonly included nutrition, adherence issues, self-management in HIV/AIDS and age-appropriate sexual and reproductive health issues. Sometimes psychosocial support entailed initiating child protection procedures involving legal assistance for OVC, when necessary.

Patients have been followed up through regular monthly visits since starting the project, either at the outreach clinics or at the Home Care Department. As part of the follow up process, pre-ART patients were home visited to map their homes for future visits, assess psychosocial issues that could affect adherence during pre-ART preparations, and evaluate the need for other psychosocial support services. Home visiting provided vital first hand impressions about the homes and family settings of the children and adolescents visited. The strategy was also used to track defaulters.

ART care package

Generally, ART care was an "add-on" to the pre-ART care package described above. All eligible patients and their care givers were taken through two to three weeks of pre-ART preparations before starting ART. Issues with disclosure, drug stock-outs and other logistic challenges may have delayed ART initiation. Follow up visit schedules for clinical evaluation and laboratory tests for ART patients were similar to pre-ART patients. Additional tests were performed anytime if clinically required.

Generally, patients on ART had a more aggressive tracking through phone calls and home visits, when they missed appointments or when treatment failure was suspected. Such patients received additional adherence support counselling and other forms of support depending on the needs and available resources. For example, health care providers also made efforts to build family support for therapy. In special cases, the outreach team delivered ART and food supplements to patients in their homes to promote adherence and improve treatment outcomes. Such special cases usually involved orphans and vulnerable children with little or no social support networks. Although such services were usually provided on a monthly basis, the frequencies depended largely on the needs and available resources.

Data collection system

Data collection involved different categories of health workers, different types of data and data collection tools, and selective linkage of data from paper-based registers and patient files to an electronic database, all of which were associated with challenges.

Patient data were routinely collected by attending clinicians, nurses, counsellors, social workers, laboratory staffs and data clerks at all five locations and recorded in physical patient files and registers or pre-designed reporting templates. Data collected included socio-demographic information, clinical records, laboratory tests and results and information on counselling and other psychosocial support services including OVC support, workshops and home visits. Data were collected during the clinics, counselling sessions, workshops, home visits and community-based activities, where community volunteers played important roles in data collection, through monthly reports.

Although large amounts of data were collected, owing to design and limited capacity, it was mainly quantitative socio-demographic data, clinical records and laboratory data that were selectively entered into an electronic database by trained staffs. Such data were stored in password protected Microsoft Access files and updated on a monthly basis (Microsoft Corporation, Virginia, USA).

Generally, data collection was associated with many operational challenges, particularly documentation and capturing laboratory data. Ordering laboratory tests and receiving results entailed a complex chain of activities often involving about three different categories of staffs and a number of intermediate steps. Not all the players and intermediate steps were effectively coordinated, resulting in missing data at various points along the chain, which in turn may influence reporting.

Outcome measurements and statistical analysis

Outcomes of interest were death, LTFU, and attrition. Among patients receiving ART, LTFU was defined as no patient contact for more than 3 months before the end of the study period among patients who had not died or transferred out of care; patients not receiving ART were considered LTFU after 6 months with no patient contact. Attrition was defined as LTFU and death combined. Time to attrition was calculated as the difference between date of last patient visit, date of patient transfer to other treatment center, or date of death and date of first patient visit. One day of follow-up was added for patients with a recorded first visit but no other recorded visits or death.

Baseline characteristics were compared between groups using Pearson's χ^2 for comparisons between two binomial categorical variables and Kruskal Wallis tests for comparisons between categorical variables with two or more categories. In addition to gender, comparisons were made by age category (0-2, >2-5, >5-10, >10-15, and >15-20 years), orphan status, whether or not the child had initiated ART, and whether or not the child had recorded CD4 values within one year before to one month after ART initiation. Kaplan-Meier estimates of death, LTFU, and attrition were calculated. The logrank test was used to compare Kaplan-Meier estimates of attrition between children receiving ART and those not receiving ART.

Multivariable Cox proportional hazard regression models were used to identify predictors of LTFU or attrition among all children in the cohort and among the subset of patients receiving ART. Models were adjusted for baseline characteristics including gender, orphan status, age, BMI, CD4 count and percent, whether or not ART was received, initial ART regimen and year of ART initiation. CD4 count and percent were only included in the model among the subset of patients receiving ART, as three quarters of the full cohort were missing CD4 data while fewer (55%) were missing CD4 data among the subset of children on ART. Multiple imputation by chained equations (MICE) was used to estimate missing covariate values in all models. Data were analyzed in Stata version 12.0 (Stata Corporation, College Station, TX, USA).

Ethical approval

The Uganda National Council for Science and Technology granted ethical approval (Ref #: HS 1021) for the study.

Results

Baseline patient characteristics

Between October 2003 and August 2012, 1498 patients were enrolled in the Tukula Fenna project. Of the 1498 enrolled, 1162 patients had confirmed positive HIV status. Total follow-up was 3466 person-years, median follow-up time from enrollment was 24.97 months (IQR 6.21-65.61), and median follow-up time from ART initiation was 36.57 months (IQR 17.48-61.24) among the 625 patients who initiated ART.

Baseline characteristics for these 1162 patients stratified by gender are summarized in Table 1. Significant differences were found between age categories in orphan status, with higher proportions of orphans in the >5-10 and >10-15 years groups (38.10% and 36.80%, respectively) than in the 0-2 (5.02%), >2-5 (17.47%), or >15-20 (2.60%), p for trend<0.01) years age groups. In addition, median BMI z-score was lower among children>5-10 and >10-15 years old (-2.39 and -2.40 versus -0.81, -0.97, and -1.50 than those 0-2, >2-5, and >15-20, respectively, p for trend<0.01). Initiation of ART and timing and make-up of initial ART regimens also differed by age category, with a higher percentage of children receiving ART in the >5-10 and >10-15 years age groups (33.92% and 30.40% versus 13.76%, 19.84%, and 2.08% than those 0-2, >2-5, and >15-20 years, respectively, p for trend<0.01). Children in the >2-5 years age group made up a large percentage of ART recipients only in 2009-2010 (31.55% versus 16.33%, 13.29%, 17.44%, and 14.85% in 2003-2004, 2005-2006, 2007-2008, 2011-2012, respectively). On the other hand, those in the 0-2 years age group made up a large percentage of ART recipients only in 2011-2012 (28.71% versus 4.08%, 10.49%, 13.37%, and 11.76% in 2003-2004, 2005-2006, 2007-2008, and 2009-2010, respectively, p for trend<0.01). Orphans in this cohort were older (median age 8.77 years versus 4.36 years for non-orphans, p<0.01, 28.05% and 28.33% of non-orphans in 0-2 and >2-5 years age groups, respectively versus 5.02% and 17.47% of orphans, p<0.01), had lower BMI z-scores (median -2.40 versus -1.53 among non-orphans, p<0.01), and were less likely to receive ART (51.3% orphans received ART versus 59.5% non-orphans, p=0.02). In addition to orphan status and age, children receiving ART differed from those not on ART by CD4 z-score, with a lower median CD4 z-score (-0.18) among ART recipients than among non-recipients (1.28, p<0.01). Patients missing CD4 count data were more often orphans, (62.9% orphans versus 52.2% among those with CD4 data, p=0.01) and younger (median 6.27 years versus 7.21 years among those with CD4 data, p=0.02). They also weighed less (median BMI z-score -1.93 versus -1.36 among those with CD4 data, p<0.01), and were much less likely to receive ART (39.4% received ART versus 96.6% of those with CD4 data, p<0.01).

Attrition and loss to follow-up

Throughout the entire study period, 5.34% (62) of patients died, 37.61% were LTFU (437), and overall attrition was 42.94% (499). This resulted in overall incidence of death of 18 per 1000 person-years, of LTFU of 126 per 1000 person-years, and of attrition of 144 per 1000 person-years. At 12, 24, and 36 months after enrollment, mortality was 4.13%, 4.65%, and 4.99%, LTFU was 21.34%, 26.76%, and 29.52%, and overall attrition was 25.47%, 31.41%, and 34.51%, respectively. Attrition, LTFU and mortality were lower among the 625 patients receiving ART, with 12, 24, and 36 month mortality of 1.60%, 2.08%, and 2.24%, LTFU of 3.84%, 7.04%, and 8.48%, and overall attrition of 5.44%, 9.12%, and 10.72%. Figure 1 shows the Kaplan-Meier failure curves for death, LTFU, and attrition throughout the duration of the study among all 1162 patients. While mortality ceases to increase after the first year or so, LTFU and overall attrition continue to increase after 12 months, albeit at a slower rate.

Predictors of attrition and loss to follow-up

Cox proportional hazards ratios for attrition and LTFU among all patients and those receiving ART are shown in (Table 2 and 3), respectively. The single factor significantly associated with overall

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Table 1: Baseline characteristics of 1162 children enrolled in Tukula Fenna HIV programme between October 2003 and August 2012, by gender.

	Overall	Male	Female	p-value for difference¥
	n=1162 (100.00%)	n=562 (48.36%)	n=600 (51.64%)	
Orphaned*, *n* (%) (*n*=891)[1]	538 (60.38)	259 (59.82)	279 (60.92)	0.74
Age in years, *median* (IQR)	6.52 (7.31)	6.26 (7.15)	6.82 (7.40)	0.41
Age group categories, *n* (%)				0.72
0-2 years	213 (18.33)	103 (18.33)	110 (18.33)	
>2-5 years	247 (21.26)	125 (22.24)	122 (20.33)	
>5-10 years	380 (32.70)	184 (32.74)	196 (32.67)	
>10-15 years	302 (25.99)	138 (24.56)	164 (27.33)	
>15-20 years	20 (1.72)	12 (2.14)	8 (1.33)	
CD4 count± z-score, *median*(IQR), (*n*=293)[2]	-0.13 (1.61)	-0.06 (1.72)	-0.18 (1.44)	0.47
CD4 percent± z-score, *median*(IQR), (*n*=228)[3]	-0.21 (1.56)	-0.33 (1.63)	0.00 (1.61)	0.06
WHO clinical stage, *n* (%), (*n*=1158)[4]				0.28
I/II	983 (84.89)	468 (83.72)	515 (85.98)	
III/IV	175 (15.11)	91 (16.28)	84 (14.02)	
BMI z-score, *median* (IQR),	-1.74 (2.85)	-1.74 (2.88)	-1.73 (2.81)	0.21
(*n*=999)[5]				
Receiving ART, *n* (%)	625 (53.79)	302 (53.74)	323 (53.83)	0.97
Initial ART regimen by key component, *n* (%) (*n*=625)[6]				
NNRTI-based	591 (94.56)	284 (94.04)	307 (95.05)	0.58
PI-based	28 (4.48)	16 (5.30)	12 (3.72)	0.34
Including d4t	180 (28.80)	91 (30.13)	89 (27.55)	0.48
Including ZDV	407 (65.12)	200 (66.23)	207 (64.09)	0.58
Year starting ART, *n*(%), (*n*=625)[7]				0.3
2003/2004	49 (7.52)	20 (6.31)	29 (8.66)	
2005/2006	143 (21.93)	72 (22.71)	71 (21.19)	
2007/2008	172 (26.38)	80 (25.24)	92 (27.46)	
2009/2011	187 (28.68)	101 (31.86)	86 (25.67)	
2011/2012	101 (15.49)	44 (13.88)	57 (17.01)	

* Child considered orphaned if either mother or father was reported deceased at baseline
± CD4 count and percent results from within 1 year prior to or 1 month after ART initiation
¥ Pearson's chi square or Kruskal Wallis chi square tests used, as appropriate
1 missing orphan status for 271 (23.32%) of children
2 missing CD4 count for 869 (74.78%) of children
3 missing CD4% for 934 (80.38%) of children
4 missing WHO stage for 4 (0.00%) of children
5 missing BMI z-score for 163 (14.03%) of children
6, 7 missing information on initial ART regimen and year starting ART for 537 (46.21%) of children

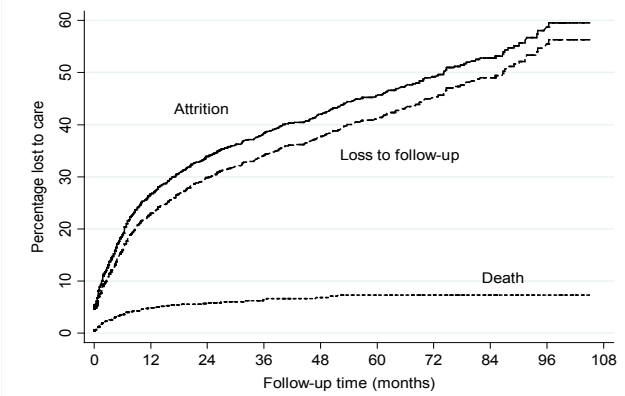

Figure 1: Kaplan-Meier failure curves for death, LTFU, and attrition throughout the duration of the study among all 1162 patients.

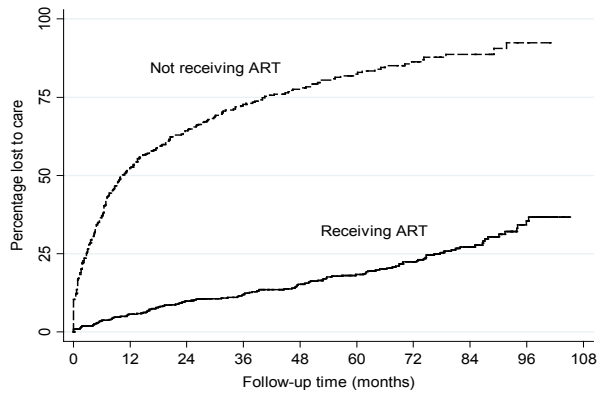

Figure 2: Kaplan-Meier failure curves for overall attrition among those patients receiving and not receiving ART.

attrition among 1162 eligible patients was absence of ART (HR: 0.11, 95% CI: 0.09, 0.14). Both BMI z-score (HR: 0.96, 95% CI: 0.91, 1.00) and receipt of ART (HR: 0.12, 95% CI: 0.10, 0.15) were significantly negatively associated with LTFU among all 1162 patients in this cohort.

Figure 2 shows the Kaplan-Meier failure curves for attrition among children who were receiving ART and those who were not yet on ART. Attrition was significantly higher among those not receiving ART (logrank χ^2=516.27, p<0.01). In the subgroup of 625 patients receiving

Table 2: Cox proportional hazard ratio of risk of attrition* among 1162 children enrolled in Tukula Fenna HIV programme and 625 receiving ART between October 2003 and August 2012.

	All patients (*n*=1 162)		Patients receiving ART (*n*=625)	
	Hazard ratio (95% confidence intervals)	p-value	Hazard ratio (95% confidence intervals)	p-value
Male	1.12 (0.94-1.34)	0.21	0.89 (0.68-1.44)	0.95
Orphaned	1.03 (0.81-1.30)	0.82	1.03 (0.65-1.63)	0.9
Baseline age in months	1.00 (1.00-1.00)	0.68	1.00 (1.00, 1.01)	0.41
Baseline BMI z-score	0.96 (0.91-1.00)	0.04	1.02 (0.92-1.01)	0.69
Baseline CD4 count± z-score	-	-	0.88 (0.61-1.26)	0.48
Baseline CD4 percent± z-score	-	-	1.03 (0.72-1.48)	0.86
Receiving ART	0.12 (0.10-0.15)	<0.01	-	-
Initial ART regimen				
NNRTI-based	-	-	Reference	
PI-based	-	-	0.87 (0.36-2.07)	0.75
Including d4t	-	-	0.69 (0.32-1.48)	0.34
Including ZDV	-	-	0.85 (0.42-1.70)	0.64
Year starting ART				
2003/2004	-	-	0.98 (0.39-2.47)	0.96
2005/2006	-	-	0.69 (0.30-1.59)	0.39
2007/2008	-	-	0.75 (0.30-1.87)	0.54
2009/2010	-	-	0.75 (0.35-1.63)	0.47
2011/2012	-	-	Reference	

*Attrition defined as death or no contact prior to August 7, 2012 for at least 6 months among children not receiving ART and for at least 3 months among those receiving ART
± Baseline CD4 count and percent results from within 1 year prior to or 1 month after ART initiation

Table 3: Cox proportional hazard ratio of risk of loss to follow-up* among 1162 children enrolled in Tukula Fenna HIV programme and 625 receiving ART between October 2003 and August 2012.

	All patients (*n*=1 162)		Patients receiving ART (*n*=625)	
	Hazard ratio (95% confidence intervals)	p-value	Hazard ratio (95% confidence intervals)	p-value
Male	1.15 (0.94-1.40)	0.09	0.98 (0.66-1.47)	0.94
Orphaned	1.11 (0.85-1.45)	0.74	1.06 (0.63-1.76)	0.84
Baseline age in months	1.00 (1.00-1.00)	0.7	1.00 (1.00, 1.01)	0.35
Baseline BMI z-score	0.97 (0.93-1.03)	0.09	1.01 (0.89-1.13)	0.91
Baseline CD4 count± z-score	-	-	0.90 (0.63-1.26)	0.52
Baseline CD4 percent± z-score	-	-	1.03 (0.71-1.49)	0.89
Receiving ART	0.11 (0.09-0.14)	<0.01	-	-
Initial ART regimen				
NNRTI-based	-	-	Reference	
PI-based	-	-	0.89 (0.34-2.30)	0.8
Including d4t	-	-	0.72 (0.32-1.62)	0.43
Including ZDV	-	-	0.87 (0.42-1.83)	0.72
Year starting ART				
2003/2004	-	-	0.76 (0.29-2.03)	0.59
2005/2006	-	-	0.52 (0.22-1.27)	0.15
2007/2008	-	-	0.68 (0.26-1.75)	0.42
2009/2010	-	-	0.73 (0.33-1.64)	0.45
2011/2012	-	-	Reference	

*Loss to follow-up defined as no contact prior to August 7, 2012, excluding any deaths, for at least 6 months among children not receiving ART and for at least 3 months among those receiving ART
± Baseline CD4 count and percent results from within 1 year prior to or 1 month after ART initiation

ART, no baseline characteristics were significantly associated with either attrition or LTFU.

Missing data

High percentages of children were missing CD4 data 74.78% (CD4 count) and 80.38% (CD4%). In addition, 46.21% of ART regimen information, 23.32% of data on orphan status and 14.03% of data on BMI z-score were missing.

Discussion

We found that among children and adolescents receiving HIV care through the Tukula Fenna project, overall incidence of death was 18 per 1000 person-years, of LTFU was 126 per 1000 person-years, and of attrition was 144 per 1000 person-years. Not receiving ART was the single factor significantly associated with overall attrition among the 1162 patients studied, while both baseline BMI z-score and receipt of ART were significantly negatively associated with LTFU among all patients in this cohort. The higher rate of LTFU and relatively lower death rate observed in this study are in line with the literature, and most likely due to considerable misclassification of LTFU, that is, many deaths among patients considered LTFU [21,22]. We also think that the high LTFU rate may be due in part to delays in obtaining and entering data, such that patients considered LTFU may actually have unrecorded visits or unrecorded deaths. A considerable proportion of attrition occurred during the first 12 months or so after enrolment into care, which is consistent with the literature [23,24] and depicted in Figure 1. Potential explanations include patient factors, such as enrolling into care with comorbidities and advanced disease, providers factors such as delayed linkage to care and or failure of timely initiation of ART in eligible patients, and health system factors such as stock-outs of drugs and poor geographical access to HIV paediatric services.

Our data also support studies that have demonstrated that ART is protective against LTFU and attrition. That is illustrated by lower rates of deaths, LTFU and attrition among patients receiving ART, compared to those not receiving ART (Figure 2) over the study period [4,25]. Children on ART may enjoy better overall health including improved growth responses [26-28], better enabling them to come in for their scheduled visits. There may also be greater motivation on the part of caregivers to promote retention in care as part of promotion of adherence to ART, such that children not on ART would not receive the extra attention paid to those on ART. Studies have also demonstrated that healthy HIV infected children have a lower risk of attrition [29,30] compared to sick and malnourished children and may explain the protective effect of baseline BMI z-scores against LTFU observed in the current study. Additionally, as described under the ART care package, the existing patient tracking system seems to favour those receiving ART, compared to pre-ART patients, due to rationing of resources. Every effort should be made to initiate ART as early as possible among HIV positive paediatric patients, as well as streamline linkage to care and tracking of HIV positive children not yet receiving ART in order to improve retention rates among this sub-group.

There were notable variations in the timing, proportions and trends in ART initiation with respect to the age categories. For instance,

children in the age group >2-5 years made up a large percentage of ART recipients only in 2009-2010, while those in 0-2 years constituted a large proportion of ART recipients mainly in 2011-2012. It is important to recognize that patients in this study have been enrolled from 2003-2012 and many changes have occurred over the period in terms of general access, treatment protocols, and in particular, eligibility for ART among children, following the serial revisions of the treatment guidelines. Thus, the observed trends could be reflecting increasing access with improvements in some services overtime, and increasing eligibility for ART associated with the serial revisions [31-35] of the guidelines (Table 1). In addition to the changes in the treatment guidelines, PMTCT / EID, programmes were introduced in the project in 2011 and may explain the observed peak in ART initiation among the 0-2 year age group by 2011-2012.

We also saw differences between orphans and non-orphans in terms of age, nutritional status and receipt of ART. Ophans were generally older, more malnourished and were less likely to receive ART. This finding could mean that, despite food incentives and the community home-based care approach, some orphans have late or limited access to ART with resultant poor growth responses. Additionally, and perhaps more importantly, this finding may be reflecting issues related to custody of some orphans in our setting. Studies conducted in Uganda and elsewhere in sub-Saharan Africa have shown that most orphans are cared for by grandmothers and or older siblings who generally have little or no formal education and usually have no training or financial support for the care and management of People Living With HIV/AIDS (PLHA) [36-39]. Furthermore, sometimes depending on the socio-cultural events in the lives of the caretakers, some orphans may have to change caretakers and or relocate to different dwelling places. These scenarios and unreliable addresses or telephone contacts make it quite difficult tracking some orphans in the communities to provide them with psychosocial supports services in real-time. There is urgent need to strengthen the orphans and vulnerable children's programme to indentify and support such children and promote their access to health care and linkage to the nutritional support clinic.

Missing data was an important challenge in this study, and the main reasons have been described under the data collection system. Further to that, certain patient characteristics seem to be at play in explaining the observed trends. For example, patients missing CD4 count data were more often orphans, younger, in poorer health (more malnourished) and were much less likely to receive ART. These patient characteristics were found to be associated with attrition in the literature [24,30,40] and may partly explain our observations. Alternatively, this finding could be reflecting poor access to HIV services among these categories of patients.

Limitations of this study include using routine programmatic data that are based on observational information for research, issues with data collection, missing data and their potential impacts on the study outcomes. Some of the challenges with observational data are that, they may not be designed to answer specific research questions, and operational definitions may not be universal, making it difficult to compare some outcomes from different studies. In addition, the scope of observational data may predispose to bias, which in turn could limit the extent to which results can be extrapolated. The current analysis has revealed important gaps in data collection, fragmented and uncoordinated data collection tools and selective linkage of mainly quantitative data from the clinics and laboratory into the electronic database. These challenges translate into poor data capturing and missing data for some variables, including those related to attrition and LTFU. Missing data about reason for exiting the programme may also contribute to these rates, as some patients considered lost to follow-up may have transferred to other facilities or tested negative for HIV after an initial positive test and terminated from care. Other studies from similar LMIC have documented the negative impacts of incorrect or missing contact information on LTFU and attrition rates [21,41].

Multiple Imputation by Chained Equations (MICE) was used to estimate missing covariate values in all models in this study. Additionally, differences in baseline characteristics were all adjusted for, in order to minimize any potential confounding.

We believe that regular training of data collecting staffs, simplifying and streamlining data collection tools, together with regular updates of patient information could improve the data capturing system and minimize missing data. In addition, including qualitative data on home visits, psychosocial support services and orphans and vulnerable children support in the electronic databases would facilitate analysis and usage of such data for research. Such a measure would explore the value of qualitative data and show how they may contribute to explain outcomes such as attrition and LTFU in this under studied population. Despite the limitations, we believe that our findings remain valid and relevant.

Conclusion

Overall, attrition and LTFU were relatively high in this study. Not receiving ART was the single factor significantly associated with attrition in this cohort, while both baseline BMI z-scores and receipt of ART were protective against LTFU among HIV positive children and adolescents enrolled in the Tukula Fenna project. Efforts should be made to initiate ART among all paediatric patients as soon as possible, and to provide aggressive follow-up for those not yet receiving ART. Orphans need more nutritional support to reduce the burden of malnutrition and improved access to early ART, which could also promote growth responses in this vulnerable and understudied group.

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