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CHARACTERISTICS OF HIV-INFECTED CHILDREN SEEN IN WESTERN KENYA
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ABSTRACT

Objectives: **To describe the characteristics and outcomes of children registered for care in a large HIV care programme in Western Kenya.**
***Design*: A retrospective descriptive study.**
Setting: **USAID-AMPATH HIV clinics in health centres; district and sub-district hospitals; Moi Teaching and Referral Hospital in Western Kenya.**
Subjects: **HIV-infected children below age of 15 years seen in a network of 18 clinics in Western Kenya.**
***Interventions*: Paediatric HIV diagnosis and care including treatment and prevention of opportunistic infections and provision of combination antiretroviral therapy (CART).**
Main outcome measures: **Diagnosis, clinical stage and immune status at enrollment and follow-up; hospitalisation and death. Descriptive statistical analyses and chi square tests were performed**
Results: **Four thousand and seventeen HIV-infected children seen between June 2002 and April 2008. Median age at enrollment was four years (0-14.2 years), 51% girls, 25% paternal orphans, 10% total orphans and 13% maternal orphans. At enrollment, 25% had weight-for-Age Z scores (WAZ)≥ -1 and 21% had WAZ scores ≤ 3. Orphaned children had worse WAZ scores (p=0.0001). Twenty five per cent of children were classified as WHO clinical stage 3 and 4, 56% were WHO clinical stages 1 and 2 with 19% missing clinical staging at enrollment. Cough (25%), gastroenteritis (21%), fever (15%), pneumonia (10%) were the commonest presenting features. Twenty six per cent had been diagnosed with tuberculosis and only 25% started on cotrimoxazole preventive therapy (CPT). Median CD4% at enrollment was 16% (0-64%); latest recorded values were 22% (0-64). Sixty four per cent were on cART (cART+), median age at start was 5.4 (014.4 years).The median initial CD4% among cART+ was 13 (0-62) compared to 24 (0-64) for those not on ART (cART-). Median CD4% for cART+ improved to 22% (0-59); whereas cART- was 23% (0-64) at last appointment. During the period of follow-up, one fifth (19%) of children on cART were lost to follow-up compared to slightly over one third (37%) for those not on cART. Thirty four percent were hospitalised; 41% diagnosed with pneumonia. Six per cent of 4017 were confirmed dead.**
Conclusions: **HIV -infected children were enrolled in care early in childhood. Orphanhood was prevalent in these children as were gastroenteritis, fever, pneumonia and advanced immuno-suppression. Orphans were more likely to be severely malnourished. Only a quarter of children were put on cotrimoxazole preventive therapy. Children commenced on cART late but responded well to treatment. Loss to follow-up was less prevalent among those on cART.**

INTRODUCTION

In the last two decades, the Acquired Immune Deficiency Syndrome (AIDS) epidemic that is caused by the Human Immunodeficiency Virus (HIV) has swept through sub-Saharan Africa with venom. According to the UNAIDS- *www.unaids.org*- there are 33.2 million people living with HIV, 22.5 million of them being in sub-Saharan Africa and 2.5 million being children under 15 years. In 2007 alone, there were 420,000 newly infected children worldwide with 330,000 children dying (1). In Kenya, over 1.3 million people are HIV infected, including over 150,000 children. The adult prevalence has apparently declined from a high of 15% in 1998 to a current low of 7.8 % (2). Stabilised infection levels in this epidemic may be due to improved prevention but also often result from rising death rates from AIDS which conceal a continuing high rate of new infections. There are over 1,100,000 orphans in Kenya due to parental HIV-infection and death. In 2005 alone, over 140,000 people died from HIV / AIDS in the country. HIV infection is one of the top five causes of mortality in Kenya and has greatly contributed to the under-five mortality rate rising from 112 in 1998 to 120 per 1000 in 2004 (3).

HIV-related symptoms and signs are rarely present at birth, but develop over subsequent months or years (4). In about a quarter of infected children, HIV infection progresses rapidly to AIDS or death in the first year (4,5). In the remainder, it progresses more slowly, with some HIV-infected children surviving child hood (6). The proportion of patients who have rapid progression of disease is higher in children than in adults. In the European collaborative study, mortality in HIV infected infants was 15%, and mortality by the age of five years was 28%, findings similar to those in the Italian study (6). According to the European experience, the annual rate of progression to AIDS decreases after the first year to approximately 6-8%, as does the mortality rate (5,6).

The morbidities of HIV-infected children may vary by geographical location. HIV -infected children in Africa frequently suffer from pneumonia, diarrhoea, bacteremia, failure to thrive and lymphadenopathy. In Cote d'Ivoire, among 338 consecutively admitted HIV-infected children, 26% had respiratory infections and 26% had malnutrition (7). In South Africa, among 48 children with vertically transmitted HIV infection followed for 26 months, 78% had diarrhoea, 76% pneumonia and 70% lymphadenopathy. Twenty five per cent died at a mean age of 10 months (but up to 48 months); the top four diagnoses at the time of death being dirrhoea, pneumonia, failure to thrive (FTT) and severe oral thrush (8). Mortality is also consistently higher among hospitalised children who are HIV-positive than those who are HIV-negative. The mortality rate among 354 HIV positive children aged between six months and five years hospitalised in Zambia was 19%, a rate significantly higher than the mortality rate of 9% among 912 hospitalised, HIV-negative children (9).

The effect of combination antiretroviral therapy (cART) on the disease progression and outcomes of HIV-infected children in Africa has not been well-studied, in part because few children are on cART. At the end of 2006, the WHO estimated that 115,000 children had access to HIV treatment a coverage rate of about 15%. In Kenya, only about 90,000 patients are on cART, out of an eligible population of over 750,000, with only 13,000 being children (10). Thus, data on African children's cART outcomes are just beginning to accumulate. In pooled data studying 392 children on cART in resource-limited settings including Africa, the median gain in CD4% was 8.2 at 6 months (n=48, IQR: 4.8-12.6) and 10.2 at 12 months (n=12, IQR: 6.6-16.3). The median Weight-for-Age Z score (WAZ) gain was +0.89 at 6 months and +0.92 at 12 months. Mortality over time was 7.8% (11). In a study in Western Kenya, children on cART had a good response irrespective of their orphan status, with the only remarkable finding being a lag in weight gain among the orphans on cART (12).

Moi University School of Medicine, in collaboration with Moi Teaching and Referral Hospital (MTRH), has recognised the pivotal role their institutions must play in Kenya's overall response to the threat presented by HIV-AIDS pandemic. These institutions, in partnership with Indiana University School of Medicine and USAID, established the USAID-Academic Model for the Prevention and Treatment of HIV-AIDS, now known as the USAID-Academic Model Providing Access to Healthcare (USAID-AMPATH) (13). USAID-AMPATH embraces excellent patient care, education of patients, medical and nursing students, research and rural health centre participation. As Kenya implements anti-retroviral therapy in persons infected with the HIV virus, USAID-AMP A TH has provided care for over 89,000 patients, including over 16,000 children. The USAID-AMPATH cohort of patients provides an optimal setting in which to describe HIV-related outcomes for Paedriatic patients in East Africa.

We need to examine the demographic and clinical characteristics, morbidities and outcomes for HIV-infected children in East Africa. Such studies will inform strategic protocols and improve the efficacy of HIV care and management. Describing HIV-related characteristics and outcomes for our cohort of HIV -infected children will not only benefit the thousands of children followed by the USAID-AMPATH programme, but will also provide important information for Kenya, the East African region, and beyond.

The main objective of the study was to describe the demographic and clinical characteristics; diagnoses;

treatment and follow-up outcomes among a cohort of HIV-infected children in care at a large HIV care programme in Western Kenya.

MATERIALS AND METHODS

Study design: This was a retrospective descriptive study. We used prospectively collected de-identified data from the computerised medical records of HIV -infected paedriatic patients treated in the USAID-AMPATH clinical care system in Western Kenya. The study was approved by the Institutional Research and Ethics Committee of the Moi University School of Medicine and Moi Teaching and Referral Hospital (Eldoret, Kenya) and the Institutional Review Board of the Indiana University School of Medicine (Indianapolis, IN).

Study site: USAID-AMPATH operates an urban referral clinic at the Moi Teaching and Referral Hospital (MTRH) in Eldoret, Kenya, a national tertiary referral hospital serving a catchments area of approximately 13 million people. Comprehensive HIV care services for children are also provided at 17 outlying outpatient clinics (Mosoriot, Turbo, Burnt Forest, Amukura, Naitiri, Chulaimbo, Webuye, Teso, Kitale, Kapenguria, Mt. Elgon, Hen, Kabarnet, Busia, Port Victoria, Uasin-Gishu and Khuyangu), located within district hospitals and health centres throughout Western Kenya. HIV care is provided by paeditricians, medical officers and clinical officers trained and mentored within AMPATH.

Study population: Eligible patients included any child seen in any of 18 USAID-AMPATH clinics between June 2002 and April 2008 who was HIV-infected and less than 15 years of age.

Clinical procedures: Throughout the period of the study, clinicians followed detailed, locally developed protocols consistent with World Health Organisation guidelines. HIV infection was documented by DNA-PCR (Amplicor, Roche, Basel, Switzerland) for children <18 months and by two parallel HIV rapid ELISA tests using Determine and Unigold kits for children >18 months. cART was initiated for any children <6 years of age with a CD4 cell percentage of <15%, for any child >6 years of age with a CD4 count <200 cells / mm^3, and for all children with WHO clinical stages 3 or 4 or CDC stage C disease. The standard initial cART regimens used were zidovudine/lamivudine/nevirapine for those weighing <10kg or stavudinel/amivudine/ nevirapine for those weighing >10 kg. All patients were started on cotrimoxazole preventive therapy if below the age of six years. Those above six years of age with a CD4 % of less than 25% and those with WHO stages 3 or 4 were also put on cotrimoxazole. Children started on cART were seen two weeks after initiation of therapy, and then every month thereafter. During these visits, patients undergo clinical assessments, including assessment of family and social characteristics, nutritional status, the degree of immuno-suppression, current or chronic infections, dietary intake, drug/treatment history and adherence history. Laboratory investigations included routine assessment of CD4% every six months and investigations to evaluate haemoglobin level, liver, kidney functions every three months. Tests to evaluate for toxicities were performed as necessary. Loss to follow-up was defined as missing clinic appointment for more than six months for those not on cART and more than three months for those on cART. An orphan was defined as a child who had lost either both or one of the parents. Nutritional status was defined using the following categories: a weight-for-age Z score (WAZ) of $\geq$1 indicated normal nutritional status, a WAZ score of -1 to -2 indicated mild malnutrition, a WAZ score of -2 to -3 indicated moderate malnutrition, and a WAZ score of $\leq$3 indicated severe malnutrition.

Data collection and management: Clinicians completed standard initial and return encounter forms at all USAID-AMPATH clinic visits for the children (*http://amrs.iu-Kenya.org/download/forms*). The initial encounter form included standard demographic; birth and prevention of mother to child transmission prophylaxis history; dietary intake; social; physical; examination; laboratory data and medications provided including antiretroviral drugs and opportunistic infection prophylaxis. At each subsequent clinical encounter, follow-up data were collected on inter-current symptoms, medication adherence, new diagnoses, laboratory data, and modifications in medication regimens. Dedicated data entry clerks entered this information into the ambulatory USAID-AMPATH Medical Record System with data entry validated by random review of 10% of the data entered. The medical records system was MS Access-based (Microsoft Corporation, Redmond, WA) until 2006, and currently uses MySQL based database.

Statistical methods: Descriptive statistics such as mean, standard deviation, median and range were used for the continuous variables while frequency listings were used for categorical variables. The chi-square test was used to assess any association between a categorical variable and each of the independent variables, where the cell count were below 10 the Fishers' exact test was used in 2 by 2 tables. Plots were used to explore the trends of the CD4% of children over time, and this was done both overall and by orphan status, since orphan status was hypothesized to have an effect on the trend. All statistical analyses were performed using SAS Institute version 9.1. A p-value of less than 0.05 was considered significant in all analyses.

RESULTS

Data were available for 4017 HIV-infected children who were seen in the USAID-AMPATH outpatient HIV clinics from June 2002 to April 2008. The majority of patients were enrolled at the outpatient HIV clinic at the urban outpatient clinic of Moi Teaching and Referral Hospital (33%) with the remaining patients enrolled at district hospitals and rural health centres (Table 1). The median age at enrollment was 4.5 years (range: 0 years-14.2 years), with the median duration of follow-up being 15 months (range: 0.00-74 months). At enrollment, 10% of the children were less than five months old, almost 50% were between five months and five years old, and 40 % were older than five years. About half of the children were girls (51%). A total of 59% were orphaned at enrollment: 25% being paternal orphans, 13% maternal and 11% total orphans. The predominant ethnic group of the children was Luhya (32%) with the rest being Kalenjin (27%), Luo (20%), Kikuyu (10%) and others. At the time of cART initiation, more than half of the children on cART were brought to the clinic by their mothers (52%), 14% by their grandparents, 11.5% by an auntie or uncle and only 8% by their fathers. The majority of children had less than two siblings (53%), with only 14% having five or more siblings.

Table 1
Demographic characteristics of children

	No.	(%)
Gender		
Male	1959	48.78
Female	2057	51.22
Clinic		
MTRH	1307	32.54
MRHC	343	8.54
Turbo	236	5.88
Burnt Forest	219	5.45
Chulaimbo	353	8.79
Webuye	223	5.55
Kitale	345	8.59
Busia	158	3.93
Distant clinics	833	20.74
Orphaned status		
Paternal	995	24.77
Maternal	536	13.34
Total	428	10.65
Non orphaned	1145	22.73
Unknown	913	28.50
Confirmed dead?		
Yes	224	5.58
No	3793	94.42
Ever On ARVs?		
Yes	2576	64.13
No	1441	35.87
Child attended school		
Yes	882	41.25
No	247	11.55
Non-applicable	1009	47.19
Missing	1879	

Clinical status at presentation: The majority (78%) of the children over nine months of age had completed their immunisations as defined by the Kenya Expanded Programme of Immunization (KEPI) schedule. More than a quarter (25%) of the patients had normal WAZ scores at enrollment, another one quarter (26%) had mild malnutrition, 26% had moderate malnutrition, and 22% were severely malnourished (Table 2).

Table 2
Anthropometric measures (n=4017)

	No.	(%)
Age at enrolment in categories		
<5 months	410	10.60
5 months- 1 year	328	8.48
1 to 5 years	1549	40.04
5-12 years	1462	37.79
12-15 years	120	3.10
Age at start of ART in categories		
<1 year	146	5.68
1 to 5 years	1050	40.87
5-12 years	1248	48.58
12-15 years	125	4.87
WAZ score closest to enrolment (n=3724)		
≤ 3	816	21.91
-3 to -2	982	26.37
2 to -1	990	26.58
≥ 1	936	25.13
Missing	170	
WAZ score at last appointment (n=3765)		
≤ 3	535	14.21
-3 to -2	843	22.39
-2 to -1	1220	32.40
≥ 1	1167	31.00
Missing	129	

There was a statistically significant difference between the nutritional status of non-orphaned children compared to the orphaned children at enrollment (p=0.0001), with orphaned children having more malnutrition (Table 3).

Table 3
Comparing nutritional status by orphan status

Variable	Orphan No. (%)	Non-orphan No. (%)	P-value
WAZ score at first appointment	(n=941)	(n=1755)	
≤ 3	192 20.40	421 23.99	<0.0001
-3 to-2	291 30.92	417 23.76	
-2 to -1	278 29.54	434 24.73	
≥ 1	180 19.13	483 27.52	
WAZ score at last appointment	(n=948)	(n=1722)	<0.0001
≤ 3	109 11.50	305 17.21	
-3 to-2	348 26.90	376 21.22	
-2 to-l	468 35.97	523 29.51	
≥ 1	296 25.63	568 32.05	

More than two thirds of the children were either asymptomatic or mildly symptomatic at enrollment (56%), with only 26% being in WHO stages 3 and 18% in WHO stage 4 (Table 4). The most common presenting symptoms and diagnoses at enrollment were rash/dermatitis (32%), cough (25%), gastroenteritis (21%), fever (15%), pneumonia (10%), otitis media (8%), oral thrush (8%), failure to thrive (6%), and delayed milestones (2.5%). Slightly more than one quarter had been diagnosed with tuberculosis (TB) at some time point either before or after enrollment. Only one quarter (24%) had ever been on cotrimoxazole for pneumocystis carinii prophylaxis (Table 4).

Table 4
Clinical diagnoses and signs and symptoms (n=4017)

	No.	(%)
WHO staging at enrolment (n=3844)		
Stage 1	957	24.90
Stage 2	1193	31.04
Stage 3	998	25.96
Stage 4	696	18.11
Missing	173	
WHO staging at last appointment (n=3844)		
Stage 1	695	18.08
Stage 2	895	23.28
Stage 3	964	25.08
Stage 4	1290	33.56
Missing	173	
Develop TB? (n=4017)		
Yes	1083	26.96
No	2934	73.04
Develop TB? (n=1083)		
At enrolment	215	19.85
After enrolment	868	80.15
Develop TB? (n=1083)		
After ARV	174	16.07
Before ARV	559	51.62
Never on ARV	350	32.32
Hospitalisation		
Yes	778	19.38
On septrin	978	24
Over 9 months (n=3702)		
Completed immunisation		2898

Table 5
Laboratory tests

CD4% closest to enrolment (n=2975)	
Mean (sd)	17.49 (10.96)
Median (range)	16.00 (0,64)
CD4% at last appointment (n=3273)	
Mean (sd)	22.08 (10.41)
Median (range)	22.00 (0.64)
CD4 count closest to enrollment (n=3275)	
Mean (sd)	639.56 (587.58)
Median (range)	484 (0.4337)
CD4 count at last appointment (n=3317)	
Mean (sd)	815 (588)
Median (range)	703(0.4262)
WBC at closest to enrolment (n=984)	
Mean (sd)	7619 (4247)
Median (range)	6776 (102,30000)

Hgb at closest to enrolment	(n=2851)
Mean (sd)	14.55 (226)
Median (range)	10.40 (0.10.70,12100)
ALC at closest to enrolment	(n=578)
Mean (sd)	3829.58 (2898.35)
Median (range)	3310(1.58,4600)

Clinical and immunologic course: By the time of the last appointment in the database, there was an improvement in nutritional status for most children (Table 3). Orphaned children continued to be more likely to be malnourished (were time, with significantly lower WAZ scores at the most recent assessment of nutritional status (p=0.0001).

Of the 1043 diagnosed with TB, the majority (80%) were diagnosed after enrollment. The majority of the children who developed TB were diagnosed with TB prior to initiation of cART (52%) compared to 16% who developed TB while on cART.

The median CD4 count and percentages closest to enrollment were 484 (range: 1-4337) and 16% (range: 0-64%) respectively (Table 6).

The median CD4 count and percentage increased slightly when examining the most recent clinical measurement, 703 (range 1-4262) and 22% (range 0-64) respectively (Figures 1 and 2). Orphan status did not affect these trends. (Figures 3 and 4).

Figure 1
CD4 percent profile for children on ART

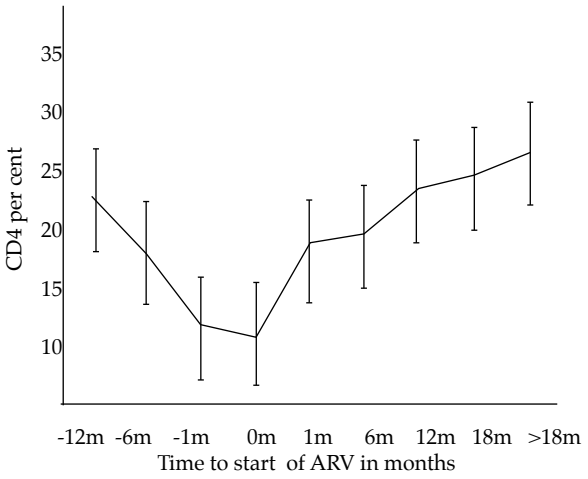
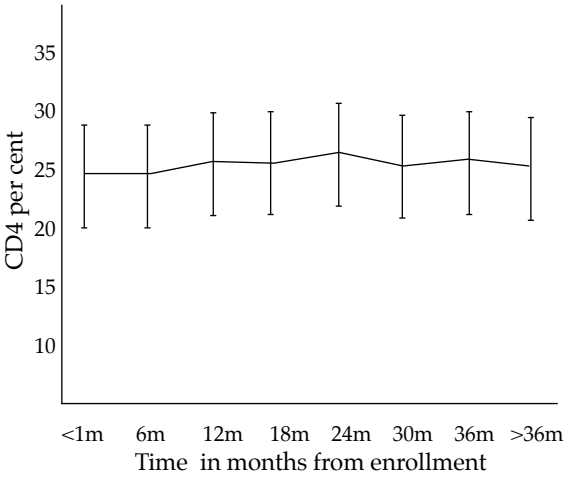


Figure 2
CD4 percent profile for children not on ART



Anti-retroviral therapy and opportunistic infections prophylaxis status: About two thirds (64%) of all HIV -infected children were on cART during the period of the study. The median age at start of the cART was 5.3 years (range: 0-14.4 years). Only 6% of the children on ART were below one year of age, 41% between one and five years, and more than half (52%) above five years.

The children started on cART had a median CD4 count and percent of 375 (range 1-4202) and 13% (range 0-62%) respectively closest to enrollment. Those not on ART had higher counts of 814 (range 0-4331) and 24% (range 0-64%) respectively closest to enrollment (Table 6). The median CD4 counts increased at the last appointment for those on cART to 671 (range 0-4262) and 22% (range 059). However, these values declined slightly in those not on cART to 787 (range 0-3940) and 23 (range 0-64) respectively. (Figures l and 2) Among those on cART, orphaned children tended to have a lower latest recorded CD 4% compared to the non-orphaned (Figure 3). The trends of CD4 percent did not vary much between the different age categories (Figure 5).

Figure 3
Median CD4 percent for those on ART by orphan status

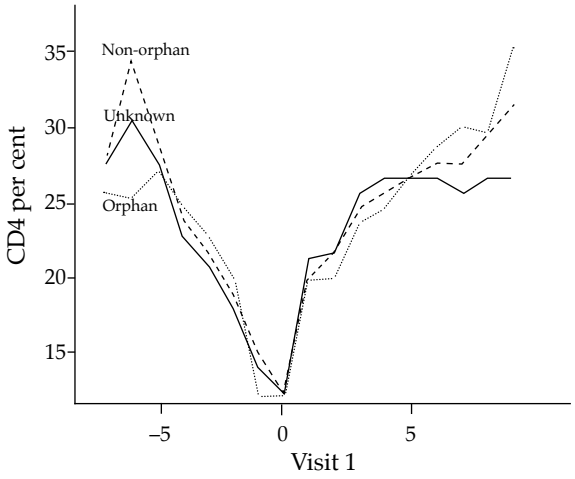


Figure 4
Median CD4 percent for those not on ART by orphan status

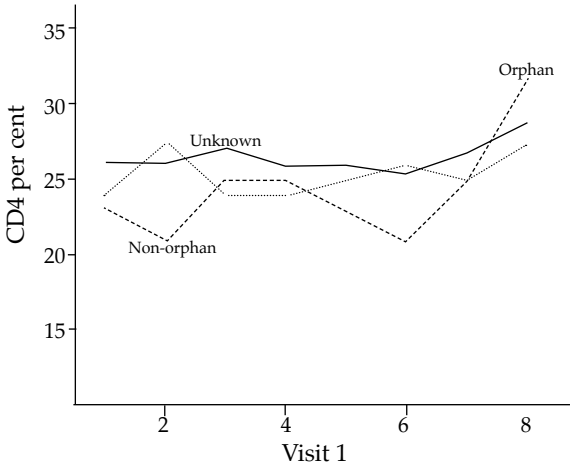


Figure 5
Median CD4 percent for children on cART with age

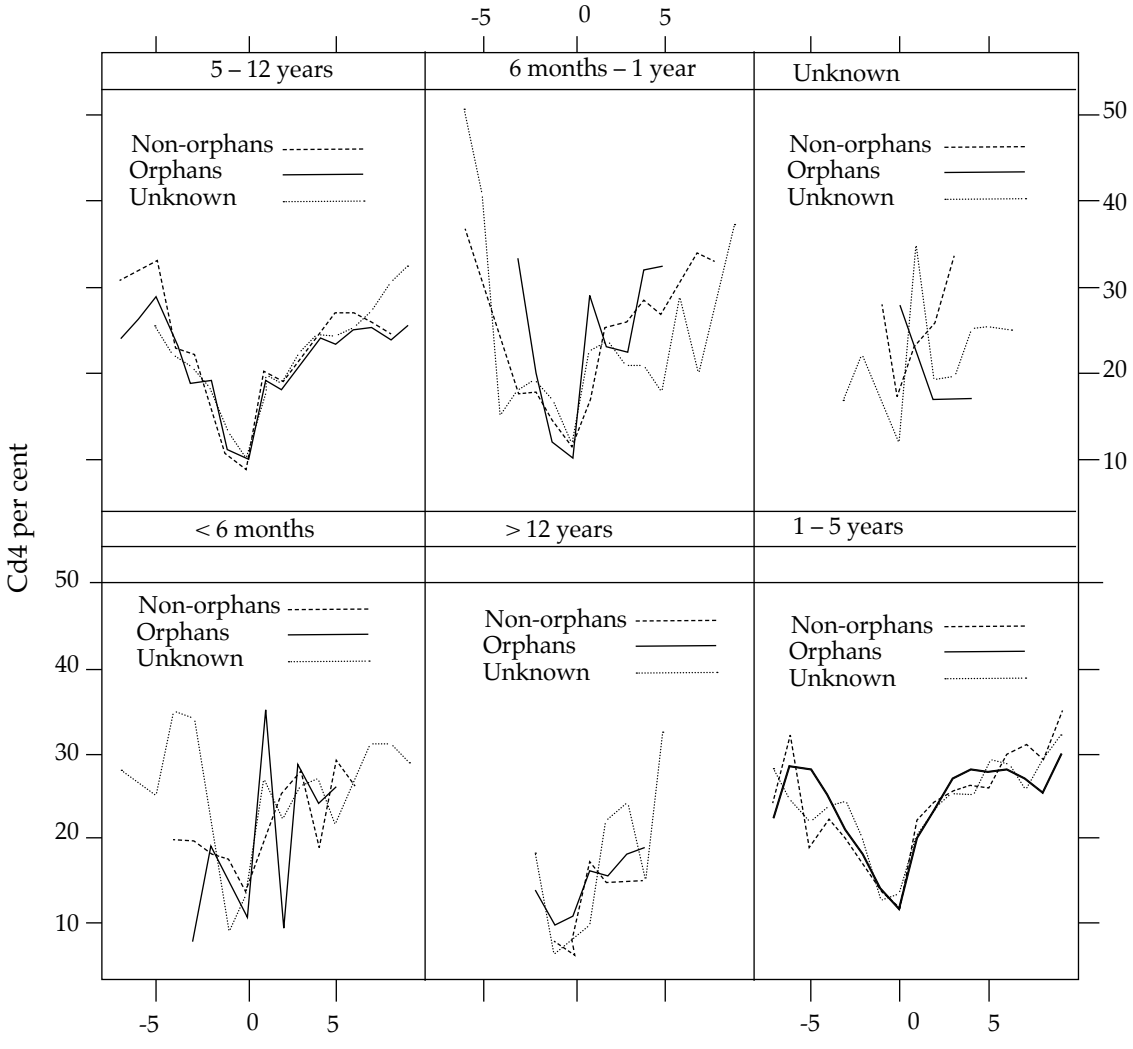


Table 6
CD4 by ARV status

	Ever on ARV	Not on ARV
CD4% closest to enrolment	(n=2107)	(n=868)
Mean (sd)	14.66 (9.84)	24.38 (10.48)
Median(range)	13.00 (0.62)	24 (0.64)
CD4% at last appointment	(n=2380)	(n=893)
Mean (sd)	21.66 (10.64)	23.20 (9.70)
Median (range)	22 (0,59.00)	23.0 (0.64)
CD4 count closest to enrolment	(n=2380)	(n=900)
Mean (sd)	505.54 (475.44)	992.93 (698.12)
Median(range)	375 (1.4202)	814 (0.4331)
CD4 count at last appointment	(n=2406)	(n=911)
Mean (sd)	768.77 (558.79)	935.01 (646.57)
Median(range)	671.5 (1.4262)	787 (0.3940)

Follow-up and admission characteristics: A quarter (26%) of the children were lost to follow-up during the duration of follow-up, with 19% of those on cART being lost to follow-up compared to slightly over one third (37%) for those not on cART. Only 6% were confirmed dead after enrollment.

About one fifth of the children (19%) were ever admitted after enrollment to various hospitals in the vicinity of AMPATH clinics during the study period. Ninety one patients were admitted to the biggest and referral facility in the programme, MTRH. Documentation for admission to other peripheral health facilities was incomplete and was not included. The most common reasons for admission at MTRH were pneumonia (n=60), malaria (n=22), pulmonary tuberculosis (n=14), meningitis (n=9), dehydration (n=9) and malnutrition (n=5). Of those admitted in MTRH, 24 died and the rest were discharged. One third (32%) of all those admitted had ever been on cART.

DISCUSSION

In this retrospective study, we describe the characteristics of a large cohort of HIV infected children in sub-Saharan Africa. The most common presenting symptoms and diagnoses in this cohort compares well with other African cohorts (8,9). Skin rash; chronic or recurrent cough probably associated with tuberculosis, lymphoid interstitial pneumonitis and upper respiratory tract infections; gastroenteritis and oral thrash formed some of the common presenting features. Interestingly, only 26% of the children seen in this cohort were diagnosed with tuberculosis before and after enrollment. This is low compared to estimated rates of TB in other children populations in Africa (9). However, this may be an indication that we are under-diagnosing tuberculosis in children, a well recognised challenge in resource limited settings where diagnostic capabilities are still limited and criteria for diagnosing TB still not well validated in the background of HIV infection (14).

A majority of the children presented at a relatively good WHO clinical stage, emphasizing the fact that our local population may be heeding the call by health personnel, community mobilisers and media for the affected families to present early for testing and care. In addition, this means that the children in our cohort are identified early for care. In contrast to early literature describing late presentation of African children (7-9), we are only seeing about 40% in WHO stages 3 and 4 at presentation. The rapid progression of HIV in children may be explained by the level of maturity of the immune system at the time of HIV acquisition. Infants with HIV are also exposed to primary infections and opportunistic organisms which is different from the reactivation of such infections that occurs in adults.

Early enrollment to paedriatic HIV care will translate to early treatment of opportunistic infections and early initiation on ART and therefore better survival (15,16). We however noted a low uptake of cotrimoxazole preventive therapy. This may be explained by the fact that almost half of the children have a good clinical and immunological status and therefore did not qualify for CPT. We have however also noted a lack of compliance to the protocols by some clinicians. This is being addressed by retraining and mentoring of the clinicians. We are also in the process of introducing electronically generated reminders to clinicians to initiate all eligible children on CPT. This will definitely help reduce the morbidity and mortality from common conditions prevalent in this population of children as has been described in Zambian children (17).

In this cohort, the majority of children receiving care in the comprehensive clinics in Western Kenya are the under-fives, indicating the increased ability of prevention of mother to child service and other entry

points in identifying the infants early and starting them on co-trimoxazole and follow-up. This might explain the relatively low crude mortality in this cohort. Early infant diagnosis is known to prevent morbidity and mortality as has been described in studies in South Africa and Uganda (15,19). In the AMPATH programme, the pMTCT programme was ramped up in 2002-2004 leading to early clinic attendance in index children and their siblings (13). We therefore demonstrate that it is possible to diagnose these children early despite the often reported delays in early diagnosis in resource limited settings. The use of all points of entry including ante natal clinic, outpatient clinics, TB clinics and wards for paedriatic diagnosis is not reported in many care settings. In Uganda and South Africa (18,19) efforts in ANC and outpatient clinics reported improvements in the rate of early diagnosis comparable to what we find in this study. More resources and targets need and can be set aside to achieve this lifesaving objective in programmes in low income countries.

The immunologic status of the children was also relatively good unlike the findings of the adult population in the same care and in other studies in Africa (20). Immunologic status was lower at enrollment for those started on ART. The median CD4 count and percentage was lower when we looked at the most recent counts for those not on ART and, as expected, was higher in those on ART in recent counts. This suggests the success of ART in this cohort, and matches the previous analyses of an earlier cohort (12) and other African cohorts (20). The trends of CD4 percent in different age categories did not vary much (Figure 5). One would have expected a more rapid decline for those below one year of age. This is perhaps explained by the consistent follow-up, prevention and treatment of opportunistic diseases in these children thus maintaining a relatively good CD4 percent.

The nutritional status of the children was relatively good at enrollment. It was significantly lower at enrollment for those who subsequently began ART. The status was also significantly lower among orphaned children compared with the non-orphaned, a feature that has been noted in an earlier cohort in the same programme on ART (12). In that study, the orphaned children seemed to lag in improvement of their nutritional status compared to the non-orphaned after 100 weeks of follow-up. In the current analysis, nutritional status improved in both groups albeit a small lag of the latest values for the orphaned on cART, which may reflect the impact of nutritional support for families that is now provided in this programme (13). In this nutritional programme, children with malnutrition or food insecurity as assessed by the nurses or nutritional assistants at each visit are initiated on food rations that include pulses and oil (provided by World Food Program) and vegetables (provided from USAID-AMPATH demonstration farms) until there is improvement in the nutritional status and food security situation. This is an important finding that requires more investigation on the effect of good nutrition in delaying initiation of ART in children.

The median haemoglobin level at enrollment in this cohort was relatively high at 10gm/dl. This is a reassuring finding in such a young population, particularly since a significant number of the children are using zidovidune, a potential bone marrow suppressant. In addition, the median white cell count and absolute lymphocyte counts were relatively high, though lower in the group that was started on ART. There were no significant differences in the absolute lymphocyte counts from different geographical and therefore ethnic sites, as contrast to findings in the adult population in the same programme (unpublished data, under review at EAMJ).

Less than one quarter of the patients were ever admitted to hospital. The most common reasons for admission of the cohort seen at MTRH were pneumonia, gastroenteritis, malaria, pulmonary tuberculosis and meningitis. These findings are similar to those in other African countries (8,9,20,21). Mortality was low in this cohort, reflecting relatively good care in a resource-constrained setting. However, there is a high loss to follow-up, and it is difficult to say whether some of these might be unreported deaths. The children on cART are less likely to be lost to follow-up and this is probably evidence of sustained education, support and follow-up that is accorded to children on cART by the caregivers and care providers. The difficulty associated with inability to trace our patients is a common feature in Africa where homes do not have well defined location. This is however being addressed in an outreach programme within USAID-AMPATH, and we hope to have less loss to follow-up and better data on mortality form this cohort in the future.

The majority are brought to the clinic by their mothers as is cultural in African countries. However, the grandparents, aunts and uncles also playa key role in bringing HIV infected children for care in those that are orphaned. This has been described in other African cohorts where the extended families have been able to lessen the burden that the orphans would otherwise face (22). More than two thirds of the children seen in this cohort are orphaned, with more than 10% having both parents' dead. This is consistent with the high prevalence of orphan-hood within Kenya. Other studies in African countries report higher rates of orphan-hood (22). Within this population, more children have lost their fathers than their mothers. This may reflect that women seek healthcare earlier than men as reported in WHO bulletins. In addition, the higher prevalence of paternal orphans may spring from earlier HIV infection, progression, and death among men compared to women (22).

This cohort describes findings in children that have access to a comprehensive package including nutritional support, micro-enterprise programmes to families to facilitate income generation, and free drugs, including ART and drugs for opportunistic infections. It may therefore not be representative,

at least in terms of disease progression in other resource-limited settings, including those run by the Kenyan Ministry of Health. In addition, the high rate of LTFU may affect the findings of this study.

In conclusion, we note that HIV -infected children were enrolled in care early in childhood. Orphanhood was prevalent in these children as were gastroenteritis, fever, pneumonia and advanced immuno-suppression. Orphans were more likely to be severely malnourished. Only a quarter of children were put on contimoxazole preventive therapy. Children commenced on cART late but responded to treatment well. Loss to follow-up was less prevalent among those on cART.

We recommend long term follow-up of children in this and other similar settings to determine the natural progression for those on ART and those not on ART. The nutritional status of orphaned children needs to be assessed more aggressively and managed early. Efforts to increase uptake of cotrimoxazole preventive therapy and decrease the loss to follow-up need to be intensified.

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