Effectiveness of Antiretroviral Therapy in Treating Paediatric HIV/AIDS in Jamaica

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ABSTRACT

Background and Purpose: *Paediatric HIV/AIDS remains a significant challenge in developing countries. We describe the effectiveness of interventions in HIV-infected children attending Paediatric Infectious Diseases Clinics in Jamaica.*

Methods: *One hundred and ninety-seven HIV-infected children were followed prospectively in multicentre ambulatory clinics between September 1, 2002 and August 31, 2005, in the Kingston Paediatric and Perinatal HIV/AIDS Programme, Jamaica, and their outcomes described.*

Results: *Median follow-up was 23 child-months (interquartile range [IQR] 12–31) with 12 children (6.0%) lost to follow-up and deaths (n = 13) occurred at 4.64 per 100 child-years of follow-up. Median age was 5.0 years (IQR 2.2–8.1) and 32.1% had Centers for Disease Control and Prevention (CDC) category C disease at enrolment; 62% were ever on antiretroviral therapy (ART) with median duration of 15.4 months (IQR 5.5–25.5); 85% initiated ART with zidovudine/lamivudine/nevirapine. Mean weight-for-height 0.13 ± 1.02 (mean difference -1.71 [95% Confidence interval (CI) -2.73, -0.69];* p = *0.001) and body mass index-for-age 0.05 ± 1.11 (mean difference -1.11, [CI -1.79, -0.43];* p = *0.002); z scores increased after 24 months on ART; however, children remained stunted. Reductions in the incidence of hospitalizations (mean diff 30.95, [CI 3.12, 58.78];* p = *0.03) and in episodes of pneumonia, culture-positive sepsis and tuberculosis occurred in those on ART.*

Conclusions: *A successfully implemented ambulatory model for paediatric HIV care in Jamaica has improved the quality of life and survival of HIV-infected children.*

Efectividad de la Terapia Antiretroviral en el Tratamiento del VIH/SIDA Pediátrico en Jamaica

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RESUMEN

Antecedentes y Propósito: *El VIH/SIDA pediátrico sigue representando un desafío mayor en los países en vías de desarrollo. Describimos la efectividad de las intervenciones en niños infectados con el VIH, que asisten a las clínicas de enfermedades infecciosas en Jamaica.*

Métodos: *Ciento noventa y siete niños infectados con el VIH fueron objeto de un seguimiento prospectivo en las clínicas ambulatorias multicentros, entre septiembre 1 de 2002 y agosto 31 de 2005, como parte del Programa VIH/SIDA Prenatal y Pediátrico de Kingston, Jamaica, y se describen los resultados.*

Resultados: *El seguimiento medio fue de 23 meses-niño (rango intercuartil [IQR] 12–31) con 12 niños (6.0%) perdidos al seguimiento y las muertes (n = 13) ocurridas en 4.64 por 100 años-niño de seguimiento. La media de la edad fue 5.0 años (IQR 2.2–8.1) y 32.1% tuvieron enfermedades de*

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categoría C en Centros de Control y Prevención de las Enfermedades a la hora de su enrolamiento, 62% estuvieron siempre bajo terapia antiretroviral (TAR) con una duración promedio de 15.4 meses (IQR 5.5–25.5); 85% iniciaron TAR con zidovudina/lamivudina/nevirapina. El peso medio por altura fue 0.13 ± 1.02 (diferencia media -1.71 [95% intervalo de confianza (CI) -2.73, -0.69]; p = *0.001) y el índice de masa corporal por edad 0.05 ± 1.11 (diferencia media -1.11, [CI -1.79, -0.43];* p = *0.002) las puntuaciones z aumentaron luego de 24 meses bajo TAR.; sin embargo, los niños permanecieron raquíticos. Reducciones en la incidencia de hospitalizaciones (diferencia media 30.95, [CI 3.12, 58.78];* p = *0.03) y en los episodios de neumonía, sepsis probada por cultivo positivo, y tuberculosis, ocurrieron entre aquellos que se hallaban bajo TAR.*

Conclusiones: *Un modelo ambulatorio exitosamente implemente para la atención pediátrica del VIH en Jamaica, ha mejorado la calidad de vida y la supervivencia de los niños infectados con el VIH.*

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INTRODUCTION

Paediatric HIV remains a significant challenge in the developing world despite tremendous successes of prevention and therapeutic interventions in developed countries. Africa continues to be the global epicentre of the epidemic. Worldwide, infected infants and children remain vulnerable through lack of access to healthcare (1, 2) except in resource-rich settings. Children now account for approximately 14% of AIDS deaths and 90% of children with HIV are in Africa. Access to antiretroviral therapy has been expanding in middle- to low-income countries but treatment and care of children continue to lag behind the developments in the adult population. The percentage of children receiving antiretroviral therapy (ART) is less than that documented for adults, a median of just 8% in Sub-Saharan Africa and in low- and middle-income countries such as in Latin America and the Caribbean (3).

In Jamaica, the HIV epidemic originated among migrant farm workers, men who have sex with men and commercial sex workers (4). Paediatric HIV was first recognized in Jamaica in 1986 (5) and the epidemiologic trend has since mirrored the increasing incidence of HIV infection in the adult population (6).

During the early stages of the epidemic, paediatric HIV care in Jamaica was primarily hospital-based, centred on acute care and palliative management and supervised by healthcare personnel who had limited therapeutic and laboratory capacity to adequately manage these children. Care in the ambulatory setting focussed on prophylaxis with trimethoprim-sulfamethoxazole (TMP/SMX) for *Pneumocystis jirovecii* pneumonia (PCP) and other opportunistic and bacterial infections and primary care management (immunization, nutrition, growth and development). Very few children were initiated on antiretroviral therapy, since the cost was prohibitive and paediatric preparations virtually non-existent. Access to care was also physician-specific and lacked the interdisciplinary approach that could enhance optimal continuity.

In 2002, the Kingston Paediatric and Perinatal HIV/AIDS Programme (KPAIDS) was initiated as a multidisciplinary collaboration between the University of the West Indies, the Ministry of Health, Jamaica, Elizabeth Glaser Paediatric AIDS Foundation and Pfizer Foundation (7). Using a public health approach (8), the primary programme aims were prevention of mother-to-child transmission of HIV and improving the quality of life and survival of already infected children and adolescents (7, 9–14). With additional support from the Clinton HIV/AIDS Initiative and the Global Fund, increased public access to antiretroviral therapy and laboratory monitoring became possible beginning in 2003.

We proposed to characterize the effectiveness of interventions in the cohort of HIV-infected children and adolescents attending four Paediatric HIV Clinics in KPAIDS and determine outcomes of enrolment, uptake of antiretroviral therapy (ART), hospitalizations, bacterial and opportunistic infections, growth and mortality.

SUBJECTS AND METHODS

Setting

Jamaica is a lower middle income state in the Western Hemisphere with a population of 2.6 million and Gross National Income per capita of US $3430 (15). The annual birth cohort of 52 000/year accounts for a HIV seroprevalence of 1.5% among pregnant women (6). Cumulatively, 799 paediatric AIDS cases (< 1 to 9 years) have been reported, of whom at least 50% have died (6). The capital, Kingston, has a paediatric AIDS rate of 265.9 per 100 000 population.

Since 2002, the Kingston Paediatric and Perinatal HIV/AIDS Programme began ambulatory management of HIV-infected infants and children attending Paediatric HIV Clinics in the Greater Kingston Region. These clinics were located at the University Hospital of the West Indies, Bustamante Hospital for Children, Comprehensive Health Centre and Spanish Town Hospital. Through outreach and preceptorship training, other clinics were established in major clinical centres throughout the island.

Design

This is a prospective, observational cohort study involving ambulatory management of infants and children attending

four Paediatric HIV Clinics in the Greater Kingston Region of Jamaica.

Participants

Infants and children were consecutively enrolled during the period September 1, 2002 to August 31, 2005. HIV infection was confirmed in children between 18 months to 18 years of age who were HIV antibody-positive by a commercial enzyme-linked immunosorbent assay (ELISA) and confirmatory test (Western blot technique). Children < 18 months of age born to a HIV-infected mother were considered HIV-infected if symptomatic of criteria for acquired immunodeficiency syndrome (AIDS) diagnosis based on the 1987 AIDS surveillance case definition (16) and/or if confirmed by positive HIV polymerase chain reaction test (Roche® DNA Amplicor PCR test). No children < 18 months who were diagnosed presumptively were later found to be HIV uninfected.

Procedure

A multidisciplinary approach to hospital-based and ambulatory treatment and care was developed (7) and key components included the training of a team of healthcare personnel, development of unified treatment and management protocols, facilitated access to care and implementing monitoring and evaluation mechanisms (9–11). Although interventions were primarily ambulatory-based, in-hospital consultations and interdisciplinary consultations were also facilitated. A public health approach to management was adopted, integrating with existing resources; interventions included (i) immunizations according to the recommended schedule of the National Expanded Programme on Immunizations (these include diphtheria, tetanus, pertussis, polio, *Haemophilus influenzae* type B, hepatitis B, measles, mumps and rubella vaccines; bacille Calmette-Guérin vaccine is given to all infants at birth), (ii) TMP-SMX prophylaxis and treatment of opportunistic infections, (iii) monitoring nutrition, growth, development and clinical progression, (iv) initiating and monitoring antiretroviral treatment according to World Health Organization (WHO) guidelines (8), (v) adherence monitoring (ART, prophylaxis for opportunistic infections, immunizations, outpatient visits, risk reduction interventions among adolescents), (vi) counselling and psychosocial support. Using the multidisciplinary team (doctors, nurses, pharmacists, social workers, adherence counsellors) ongoing adherence monitoring by self-report and pharmacy refills was conducted at each ambulatory encounter and through telephone follow-up calls. Team consultations were convened to discuss and propose solutions for challenging situations.

Primarily clinical criteria were used for initiating ART (8, 10, 11) since surrogate immunological parameters (lymphocyte subsets) did not become available until 2003 on a phased basis through the National AIDS Programme. These clinical criteria included: any child 18 months and older presenting with WHO Stage 4 (or CDC category C) disease with encephalopathy, failure to thrive or recurrent severe bacterial infections; and WHO Stage 3 (or CDC category B) disease with tuberculosis, recurrent hospitalizations due to HIV-related illness and pneumonia; children < 18 months of age with symptomatic HIV disease were initiated on ART regardless of WHO Stage (or CDC category). When immunological parameters became available, $CD4^+$ guided criteria were used to commence ART in any child with CDC immune category 2 or 3, regardless of CDC clinical category. The only available paediatric antiretroviral formulations were zidovudine, lamivudine and nevirapine. Adult preparations (zidovudine, nevirapine, lamivudine, abacavir, didanosine) and generic fixed dosed coformulations were utilized in older children. The standard first line highly active antiretroviral regime was zidovudine, lamivudine and nevirapine. Data continually tracked and audited included morbidity, mortality, hospitalizations, laboratory markers (haematology, biochemistry, cultures, immunology, lymphocyte subsets and plasma HIV-RNA).

Data were uploaded to a secure central database (7, 10) which was password protected. Outcomes evaluated were enrolment, the demographic, clinical, immunological and virological profile of the cohort, uptake of antiretroviral therapy (ART), growth, morbidity, mortality and incidence of hospitalizations, bacterial and opportunistic infections. Growth was monitored using the Centers for Disease Control and Prevention (CDC) 2000 growth charts (17).

Definitions

Lost to follow-up was defined as a client who missed two or more consecutive clinic appointments and was no longer contactable or traceable. Deceased children and those who had migrated (internal or external) were excluded from this definition. Infants and children whose care was supervised by their biological parent(s), other family members (*eg* grandmother, aunt) or foster parent received family-based care. Infants and children residing in facilities managed by community-based organizations and whose care was supervised by trained caregivers received institution or residential care.

Statistical Methods

Data were summarized and analyzed using SPSS 12.0 for Windows. Growth parameters (weight-for-age, height-for-age, weight-for-height, body mass index (BMI)-for-age) were standardized to z scores using 2000 CDC growth reference (Epi Info™ Version 3.3.2). Independent group T-tests were used to examine for differences in growth parameters (z scores) following initiation of ART compared to baseline values. Differences in mean CD4 per cent by cohort year were explored using Analysis of Variance (ANOVA). A p value of < 0.05 for 2-sided tests was considered to be statistically significant.

RESULTS

Enrolment profile

One hundred and ninety-seven children and adolescents were consecutively enrolled during the period September 2002 to August 2005. The median number of new patients enrolled per quartile was 13.0 (IQR 6.0 – 24.5; range 2.0 – 28.0). Enrolment was greatest in Year 1 (87, 44%) of the programme and subsequently decreased (Year 2 – 65, 33%; Year 3 – 17, 9%). Twenty-eight (14%) infected children were being managed in the ambulatory setting prior to the implementation of KPAIDS and were immediately enrolled at the inception.

The median duration of follow-up was 23 months (IQR 12–31 months). The total patient time of follow-up was 4340 child-months (280 child-years). Deaths (n=13) occurred at 4.64 per 100 child-years of follow-up and 12 children (6.0%) were lost to follow-up. Seven transferred to clinic sites at other locations in Jamaica and two migrated overseas.

Demographic profile

Fifty-five per cent (109; $p = 0.08$) of the cohort was female (Table 1). At enrolment, the median age was 5.0 years (IQR 2.2 – 8.1) and 131 (66.5%) were between 1 – 9 years of age. A hundred and seventy-five children (88.8%) were perinatally infected but 14 (7.1%) had acquired HIV infection *via* the sexual route (consensual or forced), three (1.5%) through transfusion and five (2.5%) by unknown means (Table 1). A hundred and fifty-two (77.0%) were receiving family-based care; the other 45 (23.0%) resided in an institution operated by a community-based organization. The children accessed ambulatory care at the University Hospital of the West Indies (101, 51.5%), the Bustamante Hospital for Children (64, 32.6%), Comprehensive Health Centre (18, 9.2%) and Spanish Town Hospital (13, 6.6%).

Clinicopathological profile

At enrolment, 63 (32.1%) of the cohort had CDC category C disease [AIDS] (Table 1). The median $CD4^+$ per cent increased by year of follow-up (Table 2). There was no significant difference in mean $CD4^+$ per cent by follow-up year (mean square = 257.56, F = 1.11; $p = 0.318$, ANOVA). There was no significant difference ($p = 0.563$) in CDC clinical category between children with perinatal *versus* non-perinatal acquisition of HIV at enrolment, however children with perinatal infection were more likely to progress to severe disease compared to children with non-perinatal acquisition of HIV ($p = 0.033$). There was no significant difference in $CD4^+$ count ($p = 0.337$) by mode of transmission.

Public access to viral load (plasma HIV RNA) testing only became available in 2005. Median plasma HIV-RNA was 23 000 copies/ml (IQR 61 – 96 000 copies/ml) among 49 children on ART. Twenty-eight per cent (14/49) had plasma HIV RNA levels less than 400 copies/ml.

ART uptake

The uptake of children on highly active antiretroviral therapy (HAART) cumulatively increased during the follow-up period. Sixty-two per cent (122/196) initiated antiretroviral therapy and 85% (104) commenced nevirapine on a nucleoside reverse transcriptase (NRTI) backbone of zidovudine and lamivudine (the only available paediatric preparations). Few children were commenced on triple NRTI (10/8%) or

Table 1: Characteristics of cohort

Variable	Baseline (enrolment)		24-month follow-up	
	All n = 197	ART-naïve n = 74	On ART N = 54	ART-naïve n = 20
Age, years, mean ± SD	5.9 ± 4.6	5.5 ± 5.0	8.0 ± 3.7	8.5 ± 4.6
median (range)	5.0 (< 1.0 – 19.0)	4.9 (< 1.0 – 18.9)	7.0 (2.0 – 19)	7.5 (2.0 – 19.0)
Age, years, n (%)				
< 1	22 (11.2)	12 (16.4)	0 (0.0)	0 (0)
1 – 4	62 (31.5)	33 (45.2)	9 (16.7)	3 (15.0)
5 – 9	69 (35.0)	17 (23.3)	29 (53.7)	11 (55.0)
10 – 14	31 (15.7)	5 (6.9)	13 (24.1)	2 (10.0)
> 15	13 (6.6)	6 (8.2)	3 (5.5)	4 (20.0)
Gender, female, n (%)	109 (55.0)	43 (58.1)	27 (50.0)	11 (55)
CDC Category, n (%)				
N	31 (15.8)	19 (25.7)	0 (0.0)	3 (15.0)
A	57 (29.1)	26 (35.1)	7 (13.0)	8 (40.0)
B	44 (22.4)	15 (20.3)	10 (18.5)	7 (35.0)
C	63 (32.1)	14 (18.9)	37 (68.5)	2 (10.0)
Unknown	1 (0.5)	–	–	–
CD4+, mean ± SD (cells/μL)	595.0 ± 304.4*	908.9 ± 636.1†	758.8 ± 503.8	1123.4 ± 626.5

*n = 80; †n = 21

Table 2: Group $CD4_+$ per cent by cohort year

Year	n	Mean CD4 %	SD (%)	95% Confidence Interval (%)		Median CD4 %	IQR (%)
2001	11	21.6	14.0	12.3	31.0	19.0	6.3 – 31.8
2002	18	24.2	17.2	15.6	32.7	21.9	6.9 – 36.9
2003	18	21.5	15.1	14.0	29.0	17.3	7.0 – 25.6
2004	40	28.4	16.2	23.3	33.6	30.0	17.2 – 42.8
2005	123	30.2	15.4	27.5	33.0	30.8	17.5 – 44.1

protease inhibitor (PI)-based regimes (7/6%) and only one adolescent on an efavirenz-based regime. Adult antiretroviral preparations and generic fixed-dose combinations were used in children over the age of three years. At the most recent clinic visit, 80% (110/137) were still on their initial antiretroviral regime. The median duration on HAART was 15.4 months (IQR 5.5 to 25.5; range < 1 to 47.4 months).

Twenty-six (21.3%) of those on HAART required change to an alternative regime because of toxicity (13, 50.0%), clinical and immunologic failure (8, 30.8%), financial limitations (3, 11.5%) or the need for optimization (2, 7.7%). Toxicity included severe anaemia and/or neutropenia (zidovudine-induced), hypersensitivity and hepatotoxicity (nevirapine-associated). Seven children were subsequently changed to a third regime and just one to a fourth regime because of clinical and immunologic failure.

Growth

Mean baseline anthropometric parameters (z scores ± SD) prior to initiation of HAART were as follows: weight-for-age -0.86 ± 2.94, height-for-age -0.48 ± 2.56, weight-for-height -1.58 ± 2.21 and BMI-for-age -1.06 ± 1.80.

The mean weight-for-height and BMI-for-age z scores (± SD) increased to 0.13 ± 1.02 (mean difference -1.71 [CI -2.73, -0.69], $p = 0.001$) and to 0.05 ± 1.11 (mean difference -1.11, [CI -1.79, -0.43], $p = 0.002$), respectively after 24 months on HAART. There was overall improvement in weight-for-age z scores (-0.70 ± 1.33, mean difference 0.16 [CI -1.12, 0.81], $p = 0.789$) following initiation of HAART but children remained relatively stunted (height-for-age z score -1.03 ± 1.50, mean difference -0.55 [CI -0.40, 1.50], $p = 0.256$).

Hospitalizations, bacterial and opportunistic infections

There were 7220 admission days and median hospitalization duration was 5.5 days (IQR 1.0 – 13.0 days). There was an overall reduction in incidence of hospitalizations (mean diff. 30.95; CI 3.12, 58.78; $p = 0.03$), bacterial pneumonia, sepsis, urinary tract infections, presumed pneumocystis pneumonia and pulmonary tuberculosis in those children who were initiated on antiretroviral therapy (Table 3). A lower incidence of hospitalizations and infection-related morbidity was also observed in those who never commenced ART compared to the incidence in the pre-ART group. Few children had documented opportunistic infections due to central nervous system (CNS) toxoplasmosis, cryptococcal meningitis, cytomegalovirus retinitis and cryptosporidiosis.

Table 3: Incidence of events per 100 child-months of follow-up

Events	Ever on ART 1030 child-months SD 12.79 n = 121		Ever on ART 2090 child-months SD 12.93 n = 121		ART-naïve 1194 child-months SD 16.36 n = 73	
	Pre-ART		Post-ART			
	# Episodes	Incidence	# Episodes	Incidence	# Episodes	Incidence
Hospitalizations	190	18.45	124	5.93*	66	5.52
Pneumonia	95	9.22	52	2.49†	11	0.92
Pneumocystis pneumonia	10	0.97	1	0.05†	3	0.25
Bacterial sepsis	26	2.52	7	0.33†	4	0.33
Pulmonary tuberculosis	11	1.07	3	0.14†	4	0.33
Urinary tract infections	32	3.11	20	0.96†	7	0.59
Cytomegalovirus retinitis	1	0.10	0	0†	0	0
Cryptosporidiosis	1	0.10	1	0.05†	1	0.08
CNS Toxoplasmosis	2	0.20	1	0.05†	1	0.08
Cryptococcal meningitis	1	0.10	0	0†	0	0

* $p = 0.03$; † p = NS

Deaths

Thirteen deaths (6.6%) occurred during the period (6 in 2003, 4 in 2004 and 2 in 2005) at 4.64 per 100 child-years of follow-up. The median age at time of death was 5.4 years (range 0.8 to 17.8). All but one had CDC category C disease. Although seven of these children were initiated on HAART, they demised within two weeks of commencing therapy. Sepsis or acute respiratory illness was implicated in eight cases and complications of HIV-associated nephropathy (three), acute gastroenteritis (one) and Burkitt's lymphoma (one) in the other five children. There was no significant difference in frequency of deaths (p = 0.369) by mode of transmission.

Characteristics of the ART- naïve children

In 74 (38.0%) children who did not initiate ART, 66 (89.2%) acquired HIV infection perinatally, seven (9.5%) *via* sexual route and one (1.4%) was unknown. At enrolment, median age was 5.5 years (range < 1.0–18.9 years) and 50 (68.5%) were between 1–9 years of age (Table 1). The frequency of most recent CDC clinical category was 11 (14.9%) category N, 22 (29.7%) category A, 25 (33.8%) category B and 16 (21.6%) category C. Median $CD4^+$ count was 788.0 cells/μL (range 39.0 – 2240.0 cells/μL; IQR 391.5 – 1246.0 cells/μL). Twenty-five (33.8%) had required hospitalization and there were seven deaths.

DISCUSSION

The implementation of the KPAIDS in Jamaica has resulted in improved growth and reduced hospitalizations, infection-related morbidity and frequency of deaths in the cohort of infants, children and adolescents followed longitudinally at four paediatric HIV clinics. These were attributed to concomitant increased uptake of antiretroviral therapy and improved immunological function in these patients. The programme has thus enhanced the quality of life and improved survival of these infected children while adopting a public health approach and integrating with existing resources in the healthcare environment.

A public-health approach to ART was adopted at inception to ensure that children would be consistently initiated on standardized, simplified, evidence-based regimes (18). Available paediatric preparations were limited in the setting and so clinicians improvised with use of adult preparations and generic fixed dose combinations. Most continued on therapy for a median of 15 months and there were no toxicity-related deaths. The advantages to this approach included dose administration convenience, preference by caregivers and children, greater acceptability compared to liquid formulations and enhanced adherence. These findings are similar to the experience in the Médecins Sans Frontières HIV programmes and in Thailand (19, 20), and support the safety and usefulness of HAART in the public-health, resource-limited setting. There are concerns regarding bio-availability and potential 'under-dosing' and 'over-dosing' with use of split tablets and emerging resistance. The cohort has the strategic option of a protease inhibitor-based regime for second line therapy in the anticipated future. With increased access to lymphocyte subsets and plasma HIV-RNA determination, the efficacy of treatment would be better characterized.

The significant improvement of growth parameters (weight-for-height, BMI-for-age and weight-for-age z scores) following initiation of HAART, clearly indicates clinical effectiveness of treatment as substantiated by paediatric cohort studies in resourceful settings (21, 22). In a similar cohort of 159 children in Abidjan, Cote d'Ivoire, in 49% initiating HAART (23), improved growth, reduced incidences of pneumonia and diarrhoea consistent with immune reconstitution and optimal viral suppression were observed. For resource-limited settings, surveillance of growth and development remain key clinical indicators of disease progression and therapeutic efficacy where capacity for laboratory monitoring may be unavailable.

Most of the children remained stunted but this may be the normal reaction to the correction of a growth-retarding disorder, that is, catch-up growth first affects weight followed by height (24). In addition, the degree of growth failure was probably significant at initial presentation, since 50% of the cohort actually presented with moderate to severe disease. Growth faltering may be related to the social environment but severity of HIV disease also affects the potential for 'catch-up' height despite use of HAART (25).

The significant reduction in hospitalizations and overall reduction in infectious events following initiation of ART further substantiates the effectiveness of therapeutic interventions (26–29) in the cohort, and is consistent with outcomes in paediatric cohorts in Thailand and Cote d'Ivoire (20, 23). In addition, all infected children in the cohort received chemoprophylaxis with TMP-SMX regardless of clinical status at enrolment until surrogate immunological markers became available. This intervention has demonstrated efficacy in reducing incidence of opportunistic and bacterial infections especially *Pneumocystis jirovecii* pneumonia (30, 31) and is congruent with recent WHO recommendations (32). The current immunization schedule in Jamaica includes *Haemophilus influenzae* type B and Hepatitis B coverage in addition to the other standard vaccines. However, none of the children was immunized against *Streptococcus pneumoniae* or influenza virus because of cost limitations. This remains a pertinent gap in prevention since pneumococcal sepsis is an important pathogen for HIV-infected children.

We were unable to adequately report on immunological and virological outcomes in the cohort since most children were initiated on HAART based on clinical criteria. This is the operational reality of many 'scale-up' initiatives where cost, capacity and access pose as barriers to these investigations. Most of the children presented between 2 to 8 years of age with approximately 50% having moderate to

severe disease at enrolment. They represented primarily slow progressors and their immunological nadir may have implications for effectiveness of antiretroviral therapy in optimally restoring immunological function (33–35). The overall improvement in $CD4^+$ per cent in the cohort suggests efficacy of treatment.

The case fatality of 6.6% in the cohort is in sharp contrast to national figures of approximately 50% in the pre-ART era in Jamaica (6). Most of the deaths occurred in children who presented at an advanced stage of disease, despite initiation with HAART, and perhaps needed palliative care. Similar findings of increased mortality in the first months of therapy are observed in other developing countries (36, 37). This is a sober reminder of the challenges facing HIV care in resource-limited settings (36), including inadequate laboratory capacity for early diagnostic testing and monitoring and access to paediatric antiretroviral formulations. A recent meta-analysis of data from resource-limited settings indicate that growth markers (*eg* weight-for-age) and haemoglobin in addition to $CD4^+$ % and $CD4^+$ count are strong predictors of mortality (38) and should be included as important variables in trials of treatment effectiveness in these settings.

Public access to antiretroviral therapy and laboratory monitoring in Jamaica has occurred on a phased basis. The process has been largely facilitated through funding by the Clinton Foundation HIV/AIDS Initiative and the Global Fund. Hence many of the children in this cohort were initiated on ART and monitored using clinical criteria (8, 10, 11). With improved laboratory capacity for monitoring the response to therapy, the efficacy of antiretroviral therapy will be more definitively characterized as the cohort matures.

In conclusion, a stable cohort of HIV-infected children and adolescents has been developed in Jamaica using a public health approach to treatment, care and support. Already other treatment sites have been established and training in Paediatric HIV medicine facilitated through preceptorship and outreach services. The conceptual and strategic framework for replication to other sites throughout Jamaica has been set. Through commitment and ongoing collaboration with other stakeholders, the vision of improving the quality of life of affected children and adolescents in Jamaica will become a reality.

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