Clinical Manifestations of Adolescents with HIV/AIDS in Jamaica

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ABSTRACT

Objective: *To characterize the clinicopathological manifestations and outcomes of a cohort of HIV-infected Jamaican adolescents.*

Methods: *This is a retrospective cohort study to determine demographic, clinical, immunological characteristics, antiretroviral uptake and mortality in 94 adolescents aged 10–19 years followed in the Kingston Paediatric and Perinatal HIV/AIDS Programme (KPAIDS) between September 2002 and May 2007. Parametric and non-parametric tests are used to compare variables.*

Results: The median age at initial presentation was 10.0 years (interquartile range (IQR) 7.0–12.0 years), 54.3% (51) were female ($p = 0.024$), transmission was primarily mother-to-child (70, 73.4%), with 87% (61) of the latter presenting as slow progressors. Sexual transmission accounted for 19.1% and there was significant female predominance (n = 15; $p = 0.024$). At most recent visit, perinatally infected adolescents were more likely ($p < 0.0001$) to reside with a non-parent (n = 42) than a biological parent (n = 19) and most had Centers for Disease Control and Prevention (CDC) category C (35/50%) disease, whereas the majority of non-perinatally infected children were classified CDC category A. Mean z scores for height-for-age was -1.47 ± 1.21 (n = 77), weight-for-age -1.06 ± 1.44 (n = 80) and BMI-for-age -0.34 ± 1.21 (n = 76) respectively; females (n = 41) were taller than males (n = 36) at their current height ($p = 0.031$). Lymphadenopathy (82%), dermatitis (72.0%), hepato-megaly (48%) and parotitis (48%) were the most common clinical manifestations, with significant predilection for lymphadenopathy ($p \# 0.0001$), dermatitis ($p = 0.010$), splenomegaly ($p = 0.008$), hepatomegaly ($p = 0.001$) and parotitis ($p = 0.007$) among perinatally infected children. Median baseline $CD4^+$ cell count was $256.0/\mu L$ (IQR 71.0 – 478.0 cells/μL); median most recent $CD4^+$ cell count was $521/\mu L$ (IQR 271.0 – 911.0 cells/μL). Seventy-six per cent (n = 71) were initiated with highly active antiretroviral therapy (HAART) and 62 (87.3%) were currently receiving first-line therapy. Six behaviourally infected females became pregnant, resulting in five live births. There were seven deaths (7.4%).

Conclusion: *This study comprehensively characterizes HIV infection among perinatally infected teens with predominantly slow-progressor disease and an increasing population of sexually-infected adolescents. As the cohort transitions to adulthood, adolescent developmental, mental health and life planning issues must be emergently addressed.*

Manifestaciones Clínicas de los Adolescentes Infectados por el VIH en Jamaica

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RESUMEN

Objetivo: *Caracterizar las manifestaciones clínico-patológicas y la evolución clínica de una cohorte de adolescentes jamaicanos infectados por el VIH.*

Métodos: *El presente es un estudio de cohorte retrospectivo con el fin de determinar las características demográficas, clínicas, inmunológicas, así como el consumo de antiretrovirales y la mortalidad en 94 adolescentes de 10 a 19 años de edad, llevado a cabo como parte del Programa VIH/SIDA perinatal y*

pediátrico de Kingston (KPAIDS) entre septiembre de 2002 y mayo de 2007. Se usan pruebas para-métricas y no paramétricas para comparar las variables.

Resultados: *La edad mediana en la presentación inicial fue 10.0 años (rango intercuartil (IQR) 7.0–12.0 años), 54.3% (51) eran hembras (p = 0.024), la transmisión fue fundamentalmente de madre a hijo (70, 73.4%), presentándose el 87% (61) de los últimos como progresores lentos. La transmisión sexual representó el 19.1% y hubo un predominio significativo de las hembras (n = 15; p = 0.024). En la visita más reciente, los adolescentes infectados perinatalmente presentaron una mayor probabilidad (p < 0.0001) de residir con personas distintas de sus padres (n = 42) que con un progenitor biológico (n = 19), y la mayor parte tenía la enfermedad categoría C (35/50%) de acuerdo con los Centros para el Control y la Prevención de las Enfermedades (CCPE), mientras que la mayoría de los niños infectados no perinatalmente fueron clasificados con la categoría A del CCE. Las puntuaciones z medias para altura por edad fue – 1.47 ± 1.21 (n = 77), peso por edad -1.06 ± 1.44 (n = 80), y el IMC por edad -0.34 ± 1.21 (n = 76) respectivamente; las hembras (n = 41) fueron más altas que los varones (n = 36) en altura corriente (p = 0.031). La linfadenopatía (82%), la dermatitis (72.0%), la hepato-megalia (48%) y la parotitis (48%) fueron las manifestaciones clínicas más comunes, con predilección significativa de la linfadenopatía (p # 0.0001), la dermatitis (p = 0.010), la esplenomegalia (p = 0.008), la hepatomegalia (p = 0.001) y la parotitis (p = 0.007) entre los niños perinatalmente infectados. La mediana de la línea de base del conteo celular CD4$^+$ fue 256.0/µL (IQR 71.0 – 478.0 células/µL); la mediana del conteo celular CD4$^+$ más reciente fue 521 /µL (IQR 271.0 – 911.0 células/µL). El setenta y seis por ciento (n = 71) fueron iniciadas con terapia antiretroviral altamente activa (TARAA) y 62 (87.3%) estuvieron corrientemente recibiendo terapia de primera línea. Seis hembras infectadas conductualmente fueron embarazadas, produciéndose como resultado cinco nacimientos. Hubo siete muertes (7.4%).*

Conclusión: *Este estudio presenta una caracterización integral de la infección por VIH entre adolescentes infectados perinatalmente predominantemente con la enfermedad de progresores lentos, y una población creciente de adolescentes infectados sexualmente. En la medida en que la cohorte transita a la adultez, el desarrollo del adolescente, la salud mental y los problemas de la planificación de la vida tienen que ser abordados con urgencia.*

INTRODUCTION

Adolescence is a dynamic period of simultaneous sexual, cognitive and socio-emotional development and is defined by the World Health Organization (WHO) as extending from age 10 to 19 years (1). In Jamaica, the adolescent population represents 20.9% of the total population (2). Globally, young people (age 15 to 24 years) account for 40% of new HIV infections in persons aged 15 years and older (3). During the period 1982 to June 2006, 11.1% of all HIV/AIDS cases occurred in the 10 to 19-year age group and 29.2% in the 15 to 29-year age group in Jamaica (4). The highest rate of newly diagnosed cases of HIV/AIDS in Jamaica has been identified as the 16 to 25-year age group with a mode of 24 years. This implies that the highest rate of HIV infection in Jamaica occurs within the adolescent period, given a range of 1 to 7 years between infection with HIV and clinical presentation and diagnosis.

During adolescence certain developmental tasks must be accomplished in order for them to achieve self-identity and become productive adults (5) and this process often involves risk-taking, pushing of limits and breaking down of barriers. During early and middle adolescence in particular, adolescents tend to be egocentric with a sense of invulner-ability and a strong desire for experimentation. These factors coupled with their newly developing capacity for abstract

thought often leads to risky behaviour with little thought given to preventive measures or long-term effects. These factors contribute significantly to how vulnerable adolescents are to the risk of acquiring sexually transmitted diseases including HIV.

There have been few studies, previously, focussing on the sociodemographic factors associated with HIV-infected adolescents in Jamaica and the Caribbean (6, 7, 8). This study aims to characterize the clinicopathological manifesta-tions and outcome of a cohort of HIV-infected Jamaican adolescents aged 10 to 19 years. Pertinent information re-garding this high-risk group is needed to assist healthcare workers in offering optimal care to the adolescents in their care.

SUBJECTS AND METHODS

Study Population
During the period September 1, 2002 to May 30, 2007 confirmed HIV-infected children and adolescents were con-secutively enrolled in the Kingston Paediatric and Perinatal HIV/AIDS (KPAIDS) Programme (9). These patients attended Infectious Diseases clinics at the University Hos-pital of The West Indies (UHWI), Bustamante Hospital for Children (BHC), Comprehensive Health Centre (CHC) and Spanish Town Hospital (STH). Most patients were referred

from within the Kingston and Metropolitan area for continued care at the ambulatory service of the respective tertiary institutions. The patients were seen by Paediatric infectious disease specialists and general paediatricians. Registered nurses specially trained in HIV/AIDS management assisted with the care and supervision of these patients (10). Although in the Jamaican public health system children are usually transferred to the adult service at age 13 years, HIV-positive adolescents continue to be followed in the KPAIDS Programme by paediatric specialists given the myriad developmental issues of adolescence that are only compounded and intensified in the presence of a chronic illness.

All confirmed HIV-infected adolescents who were between 10 and 19 years of age at any time during the period September 2002 to May 2007 were included in the study, regardless of mode of infection. HIV infection was established by a commercial enzyme-linked immunosorbent assay (ELISA) and confirmed by the Western blot technique.

Study Design and Procedures

This was a retrospective, cohort study aimed at characterizing the demographics, clinicopathological manifestations and outcome of HIV/AIDS in this adolescent population.

Participants were followed in the ambulatory setting at three-monthly intervals and management was guided by standardized protocols for clinical care, laboratory monitoring and antiretroviral therapy (ART) as previously described for the KPAIDS Programme (9,11). These included interval history, nutritional, growth and developmental assessments, physical examinations, addressing adherence with medications for prophylaxis and antiretroviral agents (11). More frequent interval visits and hospital admissions were facilitated as the situation indicated.

Growth and development were assessed at each ambulatory visit by documentation of height, weight and sexual maturity rating of clients. Blood investigations were performed six-monthly and included complete blood counts, lymphocyte subsets, plasma viral loads, liver function tests, lipid panels, serum electrolytes, creatinine and amylase, if indicated and available.

Antiretroviral medications were administered according to the national guidelines of the Ministry of Health, Jamaica (12). The standard first line regimen used in this programme included two nucleoside reversetranscriptase inhibitors (NRTIs) and one non-nucleoside reversetranscriptase inhibitor (NNRTI), typically zidovudine, lamivudine and nevirapine.

Children were considered to be either rapid or slow progressors when they exhibited clinical signs and symptoms of the disease or signs of immunodeficiency within the first four years of life and after four years of age, respectively.

Outputs and Statistical Analysis

Data were extracted from the secure KPAIDS database (9) and validated by audit of the medical records by trained medical reviewers. Relevant demographic data included age, gender, guardian status and mode of HIV infection. The key clinicopathological outcomes included HIV-related clinical signs and symptoms, growth and development, Centers for Disease Control and Prevention (CDC) clinical and immunological staging, presence of co-infections, $CD4^+$ T-lymphocyte subsets (CD4 counts) and plasma HIV RNA (viral load), antiretroviral therapy administration and mortality. CD4 count was measured with BD FACSCalibur™ system and HIV RNA was measured with Roche Cobas AmpliPrep-AMPLICOR system. Both assessments are subject to quality control using proficiency panels sponsored by Virology Quality Assessment Program, Rush – Presbyterian – St Luke's Medical Center, Chicago, Illinois, USA. The revised CDC classification system was used to describe the clinical and immunological categories of the cohort (13, 14).

Growth parameters (weight-for-age, height-for-age, body mass index (BMI)-for-age) were standardized to z scores using Epi Info™ Version 3.3.2. Independent group *t*-tests were used to examine for differences in growth parameters (z scores) by gender. Pearson chi-square, Fisher's exact test, Mann-Whitney U test, Paired *t*-test and analysis of variance (ANOVA) were used where appropriate to examine for differences by mode of transmission, gender and study duration. Data were summarized and analyzed using SPSS® 12.0 for Windows and Microsoft® Excel 2002. A *p*-value of < 0.05 for 2-sided tests was considered to be statistically significant.

RESULTS

Demographics

Ninety-four patients aged 10 to 19 years were included in the study period between September 1, 2002 and May 31, 2007. The majority were seen at the UHWI (69/73.4%) and the remainder at BHC (11/11.7%), CHC (11/11.7%) and STH (3/3.2%).

There were 43 males (45.7%) and 51 females (54.3%) (*p* = 0.024) and median age at enrolment was 10.0 years (range 2.0–18.0 years; interquartile range [IQR] 7.0–12.0 years). Behaviourally infected children were older (*p* < 0.0001) than those in other transmission groups (Table 1) but there was no significant difference in current mean age by gender (*p* = 0.61).

Mode of Transmission

Seventy children 73.4% were infected vertically *via* mother-to-child transmission (MTCT) and 36 (51.4%) were male. Of the children in the perinatally infected group, 66 (94.2%) were slow progressors, presenting after age four years. Eighteen (19.1%) children acquired HIV infection *via* the

Table 1:   Baseline characteristics at enrolment by mode of transmission

	MTCT-< 4 yr n = 4	MTCT-≥ 4yr n = 66	Sexual n = 18	Parenteral n = 2	Unknown n= 4	p value
Age (years)						
Mean	2.75	8.86	15.56	11.00	10.75	< 0.0001*
SD	0.50	2.40	2.46	2.83	1.50	
Gender n (%)						
Male	1 (2.3)	35 (81.4)	3 (7.0)	2 (4.7)	2 (4.7)	0.008[†]
Female	3 (5.9)	31 (60.8)	15 (29.4)	0 (0.0)	2 (3.9)	
Caregiver type n (%)						
Guardian	0 (0.0)	22 (84.6)	3 (11.5)	0 (0.0)	1 (3.8)	0.19*
Institution	2 (8.0)	18 (72.0)	4 (16.0)	2 (6.7)	1 (3.3)	0.13[†]
Biological parent	2 (6.7)	17 (56.7)	8 (26.7)	2 (6.7)	1 (3.3)	
Self	0 (0.0)	0 (0.0)	3 (100.0)	0 (0.0)	0 (0.0)	
Unknown	0 (0.0)	9 (90.0)	0 (0.0)	0 (0.0)	1 (10.0)	
CDC Clinical Category n (%)						
N	0 (0.0)	3 (75.0)	0 (0.0)	1 (25.0)	0 (0.0)	0.065[†]
A	0 (0.0)	28 (65.1)	13 (30.2)	0 (0.0)	2 (4.7)	
B	3 (13.6)	17 (77.3)	1 (4.5)	0 (0.0)	1 (4.5)	
C	1 (4.5)	15 (68.2)	4 (18.2)	1 (4.5)	1 (4.5)	
Unknown	0 (0.0)	3 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	
Growth (Mean z-score)						
Weight-for-age	-0.08	-1.68	-0.27	-0.36	-0.26	0.002[‡]
SD	1.46	1.43	1.37	0.64	2.57	
Height-for-age	1.74	-1.51	-0.49	-0.14	-2.48	0.001[‡]
SD	1.86	1.50	1.23	1.44	2.57	

*Kruskal-Wallis Test; [†]Mann-Whitney U Test (MTCT vs sexual group); [‡]ANOVA

sexual route and significantly more were female (15/83.3%; $p = 0.024$). Two haemophiliacs were infected parenterally *via* transfusion of infected blood products and the mode of transmission could not be determined in four patients.

Social Factors
At enrolment, 30 (31.9%) children were living with their biological parent, 26 (27.7%) with a guardian, 25 (26.6%) at a residential institution, 3 (3.2%) independently and caregiver status was unknown in 10 cases ($p = 0.13$). There was no significant change in caregiver status at the most recent clinic visit compared to that at enrolment in the programme ($p = 0.13$; paired samples *t*-test). However, among the perinatally infected children, the caregiver was more likely to be a guardian (n = 19) and an institution (n = 23) than a biological parent (n = 19) at the most recent visit ($p < 0.0001$; chi-square test).

Within the perinatally infected group, slow progressors were not likely to be living with their biological parents; 18 (27.3 %) lived in residential institutions and 22 (33.3%) with guardians. The rapid progressors were almost equally distributed between biological parents and residential institutions. Of those children infected *via* the sexual route, 3 (16.6%) were living independently, 8 (44.4%) lived with

biological parents and the remainder were equally distributed between residential institutions and guardians (Table 1).

Growth outcomes
The current mean height was 139.1 ± 1.7 cm (n = 79), mean weight was 39.2 ± 2.1 kg (n = 82) and the mean BMI was 18.8 ± 0.87 (n = 76). The mean z score height-for-age was -1.47 ± 1.21 (n = 77), mean z score weight-for-age -1.06 ± 1.44 (n = 80) and mean z score BMI-for-age was -0.34 ± 1.21 (n = 76). There was no significant difference by gender for the mean growth parameters ($p < 0.05$; independent samples *t*-test), except that females (n = 41) were taller than males (n = 36) at their current height ($p = 0.031$). Antiretroviral therapy-naïve adolescents had higher z scores for weight-for-age ($p = 0.058$), height-for-age ($p = 0.12$) and BMI-for-age ($p = 0.11$) than ART-initiated adolescents. At enrolment, perinatally infected children ($ 4 years) were significantly more wasted ($p = 0.002$) and stunted ($p = 0.001$) compared to others by mode of transmission (Table 1).

CDC classification
At the most recent visit, most perinatally infected adolescents were CDC category C (35/50%), whereas the majority of non-perinatally infected adolescents were classified CDC

category A. At enrolment, 50 (53.3%) were CDC category N and A, 22 (23.4%) CDC category B and 22 (23.4%) CDC category C (Mann Whitney U; *p* = 0.065). Among the perinatally infected adolescents, there was 54.8% increase in the proportion categorized as CDC C disease at most recent visit compared to the proportion at enrolment. This change was less evident among the non-perinatally infected adolescents.

Clinical manifestations
The most frequent clinical manifestations were lymphadenopathy (82%), dermatitis (72%), hepatomegaly (48%), parotitis (48%), splenomegaly (30%) and mucocutaneous candidiasis (23.4%). There was significant predilection for generalized lymphadenopathy (*p* # 0.0001), dermatitis (*p* = 0.010), splenomegaly (*p* = 0.008), hepatomegaly (*p* = 0.001) and parotitis (*p* = 0.007) among perinatally infected children compared to sexually-infected adolescents at presentation (Table 2).

median most recent CD4 count was 521 cells/μL (range 22.0 – 1747.0 cells/μL; IQR 271.0 – 911.0 cells/μL). There was no difference in mean baseline CD4 count by transmission mode but most recent mean CD4 count was highest (*p* = 0.017) among the perinatally infected group [$4 years] (Table 3).

Among those who were 'ever initiated' on antiretroviral therapy (71), mean CD4 count was highest among the perinatally infected group ($ 4 years) and lowest among the parenteral group at both baseline (*p* = 0.046) and most recent (*p* = 0.022) determinations. However, the lowest count (11 cells/μL) occurred in the perinatally infected group. There was significant increase in mean CD4 count at the most recent evaluation compared to the lowest value (paired samples *t*-test, *p* = 0.000), suggesting evidence of antiretroviral treatment efficacy.

Table 2:   Frequency of common clinical manifestations by mode of transmission at enrolment

Clinical Manifestations n (%)	MTCT- < 4yr	MTCT- ≥ 4yr	Sexual	Parenteral	Unknown	*p* value*
Generalized lymphadenopathy n = 77	4 (5.2)	57 (74.0)	11 (14.3)	2 (2.6)	3 (3.9)	<0.0001
Dermatitis n = 68	4 (5.9)	50 (73.5)	2 (2.9)	11 (16.2)	1 (1.5)	0.01
Hepatomegaly n = 45	2 (4.4)	36 (80.0)	5 (11.1)	1 (2.2)	1 (2.2)	0.001
Parotitis n = 45	2 (4.4)	35 (77.8)	6 (13.3)	1 (2.2)	1 (2.2)	0.007
Splenomegaly n = 28	3 (10.7)	21 (75.0)	2 (7.1)	1 (3.6)	1 (3.6)	0.008
Candidiasis n = 22	4 (18.2)	11 (50.0)	6 (27.3)	0 (0.0)	1 (4.5)	0.293
Encephalopathy n = 13	1 (7.7)	9 (69.2)	2 (15.4)	1 (7.7)	0 (0.0)	0.198
Pulmonary tuberculosis n = 9	0 (0.0)	7 (77.8)	2 (22.2)	0 (0.0)	0 (0.0)	0.622

* Fisher's exact test (MTCT *vs* sexual group)

Pulmonary tuberculosis was the most common co-infection in seven (10.6%) of the perinatally infected group and two (11.1%) of the behaviourally infected group. Five children were co-infected with hepatitis B; three of these had perinatal HIV infection, one through sexual transmission and the other parenterally. The latter was also coinfected with hepatitis C. There were single cases of cryptococcal meningitis, cerebral toxoplasmosis and progressive multifocal leukoencephalopathy. One female was diagnosed with genital herpes simplex virus Type-2 infection and there were no cases of syphilis.

Immunological and virological outcomes
CD4 counts (cells/μL) were available for 91% of the cohort (n = 82). Median baseline CD4 count was 256.0 cells/μL (range 11.0 – 1518.0 cells/μL; IQR 71.0 – 478.0 cells/μL);

Among those initiated on ART, most recent median viral load was 1340.0 copies/mL (range < 50 to > 100 000 copies/mL; n = 56). Twenty-one (37.5%) had viral loads < 50 copies/mL (17 MTCT, 4 sexual); there was no significant difference in viral load by mode of transmission (Fisher's exact test, *p* = 0.44).

Antiretroviral therapy
Seventy-six per cent (n = 71) of children in the cohort were initiated with highly active antiretroviral therapy (HAART). Fifty-three (74.6%) were perinatally infected children ($ 4 years) but there was no difference in uptake by mode of transmission (*p* = 0.35) (Table 3). Forty-one (57.7%) of them were CDC category C, 19 (26.8%) CDC B and 11 (15.5%) CDC A. Sixty-two (87.3%) were receiving first-line therapy and nine (12.7%) were on second-line regimens. The most

Table 3:   Clinicopathologic outcomes by mode of transmission

	MTCT- < 4 yr	MTCT- ≥ 4 yr	Sexual	Parenteral	Unknown	p value
Baseline CD4 count						
(cells/μL)	n = 2	n = 59	n = 17	n = 2	n = 2	
Mean	805.5	356.5	259.0	93.0	262.5	0.16*
SD	352.9	344.2	217.9	8.5	231.2	
Most recent CD4 count						
(cells/μL)	n = 2	n = 59	n = 17	n = 2	n = 2	
Mean	1268.0	634.6	432.2	93.0	516.5	0.017*
SD	691.6	412.1	281.6	8.5	128.0	
Most recent viral load						
(copies/mL x 10^3)	n = 2	n = 45	n = 14	n = 1	n = 2	
Mean	8.62	19.87	25.80	100.00	23.85	0.19*
SD	12.12	33.62	32.60	–	21.71	
ARV uptake						
n (%)	2 (2.8)	53 (74.6)	12 (16.9)	2 (2.8)	2 (2.8)	0.35[†]
Deaths						
n (%)	0 (0.0)	5 (71.4)	1 (14.3)	1 (14.3)	0 (0.0)	0.21*
Pregnancy						
n (%)	0 (0.0)	0 (0.0)	6 (100.0)	0 (0.0)	0 (0.0)	< 0.0001*

*ANOVA; [†]Fisher's exact test (MTCT *vs* sexual group)

commonly used first-line regimen was zidovudine/lamivudine/nevirapine among 48 (67.6%) of those on first-line therapy.

Among the ART-naïve children (n = 23), 15 (65.2%) were infected vertically, 6 (26.1%) sexually and for 2 (8.6%) the mode of transmission was undetermined. Most were classified as CDC category A (14/60.9%), 7 (30.4%) CDC category B and 2 (8.7%) CDC category C. Median CD4 count (n = 13) was 681.0 cells/μL (range 271.0 – 1564.0 cells/μL; IQR 534.0 – 1253.0 cells/μL).

Pregnancy
Of note, 6 female adolescents who were infected *via* the sexual route became pregnant. Five of these pregnancies were successfully completed and all five of the infants have been confirmed HIV-negative.

Mortality
There were seven deaths (Table 3) of which five were perinatally infected adolescents, one *via* sexual transmission and one parenterally (*p* = 0.21). All four perinatally infected adolescents were slow progressors and mean age was 11.0 ± 3.2 years (n = 7) at enrolment. Five of the adolescents were CDC category C at the time of death and the most recent mean CD4 count was 175.2 ± 78.8 cells/μL. Five of the six patients were initiated on HAART (4 on first-line; one on second-line), however adherence was a concern. Mean age at time of death was 12.6 ± 2.9 years and the average duration between enrolment and death was four years. Circumstances surrounding the demise of these adolescents were as follows: *Case 1* (16-year old female) succumbed from respiratory failure secondary to pneumonia; *Case 2* (12-year old female) died from complications of end stage renal failure; *Case 3* (19-year old male) died as a result of septic shock; *Case 4* (11-year old male) had end stage renal failure secondary to HIV-associated nephropathy; *Case 5* (13-year old male) was known to have CNS toxoplasmosis and died as a result of aspiration during a seizure episode at home; *Case 6* (15-year old male) died from sepsis. *Case 7* (13-year old male) died from disseminated tuberculosis.

DISCUSSION
This study characterizes the clinicopathological manifestations and outcomes, and explores the social circumstances of perinatally and non-perinatally infected adolescents attending ambulatory medical services in Kingston, Jamaica. Since the initiation of universal access to antiretroviral therapy and standardized healthcare for HIV-infected children was facilitated through the Kingston Paediatric and Perinatal HIV/AIDS Programme and the Ministry of Health, Jamaica, in 2002, improved survival of perinatally infected children has led to a maturing cohort now extending into the adolescent period (15). In addition, adolescents in Jamaica continue to be at great risk of acquiring HIV, in light of the median age at sexual initiation being 13 years in males and 15.5 years in females (16). Despite an increased perception of HIV risk among Jamaican adolescents during periods 2004, 2000 and 1996, there has been no significant change in the per cent of youths reporting multiple partners and the per cent initiating sex or age at first sex (17). Although a significant increase in condom usage at last sex was reported in males, of concern was the continued risk behaviour among female adolescents.

In this study, there was a significant female predominance among those patients infected *via* sexual transmission, mirroring the global trend in HIV infection in

females aged 15 years and older (3). However, pertinent contributing factors in Jamaica include poor condom-negotiating skills by female adolescents, early sexual initiation with older men, high prevalence of sexual abuse of adolescent females and increased detection through voluntary counselling and HIV testing for all antenatal attendees (17–19). There was no significant gender difference among the perinatally infected group, a finding similar to other studies in the United States of America (20) and Zimbabwe (21).

The most common clinical manifestations in this Jamaican cohort were generalized lymphadenopathy, dermatitis, hepatomegaly, parotitis and splenomegaly. Perinatally infected adolescents were moderately stunted and wasted at presentation. These findings are similar to a recent report of adolescents in Zimbabwe (21) of similar median age at diagnosis, except that they presented with recurrent upper respiratory tract infections, chronic diarrhoea, past tuberculosis and chronic skin condition. The Zimbabwean adolescents, however, were significantly immunosuppressed and the majority had moderate to severe clinical disease (WHO stages 3 and 4) at presentation in comparison to the adolescents in the present cohort. In addition, seventy-six per cent of the adolescents in this cohort were initiated on antiretroviral therapy, hence their current growth parameters probably reflected treatment effectiveness as demonstrated in other studies (22–26).

Of note is the presentation of asymptomatic or mild disease in the majority of behaviourally infected adolescents, a finding comparable to a previous study in the US population (27). These, in addition to 19% of perinatally infected adolescents with mild disease at presentation, highlight a growing concern of 'missed opportunities' for diagnosis in the general population of adolescents in Jamaica (28). Currently, HIV screening among adolescents is limited to antenatal attendees and high risk individuals. Undiagnosed, asymptomatic infected adolescents and youth will continue to drive the epidemic in an environment of continued risk-taking behaviour (16, 17, 28).

Few sexually transmitted infections were identified in the cohort but a comprehensive evaluation would require routine interval screening to be done, which is not currently incorporated in the programme because of resource constraints. This must be addressed expeditiously as the cohort matures and potentially be at greater risk for sexually transmitted infections and pregnancy (29). We note the pregnancies occurring among behaviourally infected adolescents and must be cognizant of the likelihood of pregnancies occurring among those in the perinatally infected group as they mature toward adulthood (30).

Perinatally infected adolescents were more likely to be residing with a non-biological caregiver at the time of presentation. Parental illness and death lead to disrupted home life, inadequate social and mental support and put the child at risk for abandonment and poverty. Although the study was limited in the exploration of psychological and social issues, the creation of orphans and the psychosocial impact of the illness on the child are well recognized (31, 32).

The deaths among the cohort of adolescents were in patients with advanced disease. These are a sober reminder that palliative care and end-of-life issues must be considered in the management of infected children and adolescents as they mature (33). The initiation of antiretroviral therapy has improved the immunological function of the children in this cohort, as evidenced by the significant increase in CD4 count from nadir values. However, ART is not a panacea and the reality of reduced life expectancy must be at the forefront of the minds of our adolescents, caregivers and healthcare personnel.

This study is limited in consideration of issues beyond the clinicopathological characterization and use and benefit of antiretroviral therapy. Pertinent issues for further evaluation must include adolescent developmental concerns, mental health, disclosure, adherence, sexuality and life planning as the cohort transitions toward adulthood (31, 34–36). Also, there was likely to be referral bias towards sicker patients and the diagnostic facilities were limited especially in delineating antiretroviral treatment efficacy.

In conclusion, this study characterizes HIV infection among adolescents in a setting with moderate prevalence of HIV infection (9). Greater recognition of the implications of undiagnosed HIV infection in older children and adolescents is needed, and services to address adolescent developmental, mental health and life planning issues are emergently needed as this vulnerable cohort continues to mature. Further research is required to guide policy and implement interventions to increase HIV testing, minimize risk behaviours in adolescents and address complications among HIV-infected Jamaican adolescents and youth.

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