HIV-related Mortality in Jamaican Children

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ABSTRACT

Objective: *Paediatric HIV is a leading cause of morbidity and mortality worldwide. We describe HIV-related mortality in a cohort of HIV-infected Jamaican children and identified factors which influenced survival.*

Methods: *A retrospective descriptive study was conducted for the period March 2003 – December 2005 at Cornwall Regional Hospital, Montego Bay, Jamaica. We summarized demographic and clinical data of deceased and living perinatally HIV-infected children and identified factors that influenced survival of rapid and slow progressors. Rapid progressors are HIV-infected children identified clinically before age 2 years and slow progressors after age 2 years.*

Results: *There were 9 (18%) HIV/AIDS-related deaths among 50 HIV-infected children of whom 23 (46%) were males and 21(43%) were AIDS orphans. Five children (10%) received ARV prophylaxis, 31 (62%) were breastfed and 39 (78%) received HAART. Surviving children displayed primarily non-AIDS defining illnesses (pneumonia and sepsis) but there was no difference in AIDS-defining illnesses among living and deceased children. The median age at diagnosis was 26 months (range 3–121; IQR 10,54). The median age at death was 30 months (range 7–122 months; IQR 17,118). Both surviving and deceased children presented with primarily moderate symptoms at diagnosis (21, 42%) and death (7, 78%). In rapid progressors, 19 of 20 (95%) on HAART remained alive and all 4 (100%) who did not receive HAART died. The mortality rate in children on HAART was 30.78 per 100 person years and 48 per 100 person years in children not receiving HAART.*

Conclusions: *HAART is the only factor identified which prolonged survival for HIV-infected children who are rapid progressors, have AIDS-defining illnesses and are orphans.*

Mortalidad Relacionada con el VIH en Niños Jamaicanos

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RESUMEN

Objetivo: *El VIH pediátrico es la principal causa de morbilidad y mortalidad a nivel mundial. El presente trabajo describe la mortalidad relacionada con el VIH en una cohorte de niños jamaicanos infectados por el VIH y factores identificados que influyeron en la supervivencia.*

Métodos: *Se llevó a cabo un estudio retrospectivo para el período de marzo de 2003 a diciembre 2005 en el Hospital Regional Cornwall, de Montego Bay, Jamaica. Resumimos los datos clínicos y demográficos de los niños infectados por el VIH, tanto de los fallecidos como de los vivos, e identificamos los factores que influyeron en la supervivencia de progresores rápidos y lentos. Los progresores rápidos son niños infectados por el VIH identificados clínicamente antes de los dos años de edad y los preopresores lentos son aquellos identificados después de los dos años de edad.*

Resultados: *Hubo 9 (18%) muertes relacionadas con el VIH/SIDA entre 50 niños infectados por el VIH, de los cuales 23 (46%) eran varones y 21(43%) eran huérfanos del SIDA. Cinco niños (10%) recibieron profilaxis ARV, 31(62%) fueron amamantados y 39 (78%) recibieron TARAA. Los niños sobrevivientes mostraron enfermedades primariamente no definitorias de SIDA (neumonía y sepsis), pero no hubo diferencia en las enfermedades definitorias del SIDA entre los niños vivos y los fallecidos. La edad mediana al momento del diagnóstico fue de 26 meses (rango 3-121; IQR 10, 54). La edad mediana al momento de la muerte fue de 30 meses (rango 7–122 meses; IQR 17 118). Tanto los niños sobrevivientes como los fallecidos presentaron síntomas primariamente moderados en el momento del*

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diagnóstico (21 para un 42%) y la muerte (7 para un 78%). En los progresores rápidos, 19 de 20 (95%) bajo TARAA continuaron vivos y el total de los 4 (100%) que no recibieron TARAA murieron. La tasa de mortalidad en los niños bajo TARAA fue de 30.78 por cada 100 años-persona y 48 por 100 años-persona en niños que recibieron TARAA.

Conclusiones: *TARAA es el único factor identificado que prolongó la supervivencia de los niños infectados con el VIH que eran rápidos progresores, tenían enfermedades definitorias del SIDA y eran huérfanos.*

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INTRODUCTION

In 2003, the World Health Organization and the Joint United Nations programme on HIV/AIDS launched a programme to provide low and middle-income countries with treatment for 3 million people with HIV infection by the year 2005. Children under age fifteen years represented 10% of those in need. Globally, this target was not met (1). Latin America and the Caribbean achieved 68% coverage over this two-year period and deaths were averted due to increased access to highly active antiretroviral therapy (HAART). In developing countries, the use of HAART has resulted in a five-fold reduction in mortality and high survival rates for children of up to 90% into adulthood (2). We describe the mortality experience of perinatally HIV-infected Jamaican children during the scaling-up period of HAART.

SUBJECTS AND METHODS

A retrospective descriptive study was conducted for the period March 2003 – December 2005 at the Cornwall Regional Hospital, a tertiary care referral centre in western Jamaica. In May 2004, the Kingston Paediatric and Perinatal HIV/AIDS Programme (KPAIDS) team established an outreach paediatric HIV clinic at this site and treatment protocols were standardized (3). The cohort included HIV-infected children diagnosed before and subsequent to the establishment of the treatment site. During this period, there was a scaling-up of prevention of mother-to-child transmission, access to immunologic and virologic markers for diagnosis and monitoring and antiretroviral therapy. HIV infection was defined according to the WHO definition (4). This period was chosen as it represented the paradigm shift of no access to universal HIV care in this region. Rapid progressors were defined as an HIV-infected child who presented clinically under age two years and slow progressors were those presenting clinically over age two years. We summarized demographic and clinical data; compared sociodemographic, maternal health status, ever breastfed, clinical and laboratory markers and opportunistic infections using chi-square analysis. Immune and clinical class were classified according to the CDC definition (5). We compared mean age at diagnosis, age at death using student's t-test stratified for living and deceased cases. We analyzed the effect of antiretroviral therapy on outcomes of rapid and slow progressors. Death rates per 100 person-years were calculated by totalling the number of person days observed from time of diagnosis to death or last follow-up. Deaths among observed patients were counted and observation time was standardized to 100 person-years. All analyses were conducted using STATA (6) version 7.

RESULTS

At the Cornwall Regional Hospital, there were nine (18%) HIV/AIDS related deaths from 50 HIV-infected children with 23 (46%) males and 21(43%) AIDS orphans. Tables 1 and 2 summarize clinical features stratified from deceased and surviving children. All 21 orphans were alive with 16 (76%) in the care of a family member. Eighteen (86%) were on HAART. Surviving children displayed primarily non-AIDS defining illnesses (pneumonia and sepsis) but there was no difference in AIDS-defining illnesses in living and deceased children. There was no difference between rapid and slow progressors in non-AIDS-defining illnesses. Rapid progressors were more likely to have HIV encephalopathy but this was not statistically significant. There was no correlation of caregiver status, breastfeeding or ARV prophylaxis with death. The median age at diagnosis was 26 months (range

Table 1: Clinical characteristics among dead and surviving HIV-infected children

	Dead	Alive	Total
ARV prophylaxis	1 (20%)	4 (80%)	5
Breastfed	4 (13%)	27 (87%)	31
Orphan*	0 (0%)	21 (100%)	21
Rapid progressor	5 (21%)	19 (79%)	24
HAART*	3 (8%)	36 (92%)	39

*$p < 0.05$

Table 2: Frequency of clinical complications among 50 HIV-infected children

Complication	Dead	Alive
Tuberculosis	1	3
PCP	1	1
Oesophageal candidiasis	3	0
Encephalopathy	2	3
Wasting syndrome	5	5
Pneumonia	2	19
Sepsis	1	12
Total	**15**	**43**

PCP = pneumocystis jirovecii

3–121; IQR 10, 54). The median age at death was 30 months (range 7–122 months; IQR 17, 118).

Table 3 compares age of diagnosis and death among clinical class and surviving and deceased children. The

Table 3: Clinical class and median age at diagnosis and death in months among 50 HIV-infected children

Class	n	age at diagnosis	n	age at death
A	11 (22%)	42 (IQR 24, 58)	0 (0%)	0
B	21 ((42%)	36 (IQR 11, 56)	7 (78%)	30 (IQR 20, 114)
C	18 (36%)	18 (IQR 5, 41)	2 (22%)	(15 mo, 108 mo)
Total	**50 (100%)**		**9 (100 %)**	

median age at diagnosis decreased with increasing severity of disease. Surviving and deceased children presented with primarily moderate symptoms at diagnosis (21, 42%) and death (7, 78%). The immune status among 37 children were 10 (27%) for class 1 (none); 12 (32%) class 2 (moderate) and 15 (41%) class 3 (severe).

Table 4 compares HAART therapy on the outcome of rapid and slow progressors. Two of the three children on

Table 4: Outcomes among 50 HIV-infected children stratified between HAART therapy and rapid and slow progressors

	+HAART		-HAART		Total
	rapid	slow	rapid	slow	
Dead	1 (5%)	2 (11%)	4 (100%)	2 (29%)	9
Alive	19 (95%)	17 (89%)	0 (0%)	5 (71%)	43
Total	20 (100%)	19 (100%)	4 (100%)	7 (100%)	50

$p < 0.0001$

HAART who died had discontinued therapy three months or more before death. The third child died within three weeks of commencing HAART. Among rapid progressors 19 of 20 (95%) on HAART remained alive and all 4 (100%) who did not receive HAART died. The mean age of death for rapid progressors was 23 ± 9 months (95% CI 11, 34) and the mean age at last follow-up for survivors were 48 ± 38 months (95% CI 30, 67). The median age at initiation of HAART was 53 months (range 4 –154; IQR 16, 95). The median duration on HAART to last follow-up was 8.4 months (range 0.15–21.8; IQR 3.9, 17.4).

The mortality rate for children on HAART was 30.78 per 100 person-years and 48 per 100 person-years among children not receiving HAART.

DISCUSSION

Paediatric HIV is a leading cause of morbidity and mortality worldwide with approximately 700 000 new cases being diagnosed annually. Fewer than 5% of those who received HAART in 2005 through the WHO 3 by 5 initiative are children (1). Children in Sub-Saharan Africa who acquire disease in utero, intrapartum or early postpartum have an increased risk of death under age two years compared to acquisition in late postpartum (7). We have examined factors influencing survival for a subset of HIV-seropositive children during the initial scaling-up period of HAART and compared outcomes of rapid and slow progressors.

These data may be biased as the mortality information was hospital-based. Children may have died at home or at other hospitals and more severe forms of the disease would have presented to hospital. A hospital-based cohort may also select families with similar health-seeking behaviours and influence interpretation of the data. Despite these limitations, the results presented here are important because they represent the first attempt to examine survival among rapid and slow progressors in the Caribbean.

Few children were diagnosed in the prenatal period resulting in few receiving antiretroviral prophylaxis, many breastfeeding and the majority of children presenting with moderate to severe symptoms. Ten years ago, children presented similarly in a hospital-based survey but the median age at death increased from 12 months to 30 months (8). This difference may have been influenced by standardized care, a change in health-seeking behaviour due to access to better care and the introduction of HAART. A similar result has been documented in the developed and developing world and is attributed to HAART and prevention of perinatal transmission (9).

In our series, approximately half of deceased and surviving children were cared for by their mothers, as the remainder had died. In Sub-Saharan Africa, children whose mothers died experienced an increased mortality risk of 57.1% compared with 12.8% for children whose mothers survived (7, 10). This was not our experience as all AIDS orphans survived likely due to the introduction of HAART. Earlier prenatal diagnosis of these children would have identified their mothers earlier, allowing maternal access to HAART and improved outcomes in children.

The surviving and deceased children had advanced HIV disease as evidenced by their primary presentation of moderate to severe immunosuppression and clinical class. Rapid progressors were more likely to have HIV encephalopathy but this difference was absent when dead and living subjects were compared due to the presence of HAART. Evidence is emerging that early antiretroviral therapy can protect the central nervous system in infants (9). More recent studies suggest that antiretroviral therapy initiated before 12 weeks of age reduces mortality by 75% in young HIV-infected infants (11). This has implications for the guidelines in commencing therapy and identifying factors to better define the short *versus* long-term survivors.

Previous studies in Jamaican children demonstrated that HAART reduces hospital length of stay, improves growth parameters, improves CD4 counts and reduces viral

load (12, 13). The effect on rapid progressors was that survivors had doubled the mean age at last follow-up compared with those who died.

The children who died were diagnosed late and two of three who had access to HAART were non-compliant for a prolonged period. Access to HAART will improve outcomes only if there is adherence to the regime. Children who are compliant have been shown to have a reduction in symptoms and death. An integrated approach in monitoring adherence is required (14). Severely advanced disease and delayed start may have precluded the benefits of HAART in the child who died within three weeks of initiating HAART.

Overall, HAART reduced the mortality rate and prolonged survival for HIV- infected children who were rapid progressors, had AIDS defining illnesses and were orphans. A greater impact is anticipated with increased access to care, earlier diagnosis and appropriate interventions.

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