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Long-term outcomes of HIV-infected children in Thailand: the Thailand Pediatric HIV Observational Database

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SUMMARY

Objective: To describe the outcomes of antiretroviral therapy (ART) in a large cohort of HIV-infected children in Thailand.
Methods: The data were obtained from four collaborative referral sites around the country. Data from 2008 to March 2011 were collected prospectively, and data before 2008 were collected retrospectively.
Results: Of the 1139 children, 599 (52.6%) were female, and the duration of ART was a median 2.9 years (interquartile range (IQR) 3.3–5.5 years). At ART initiation, the median age was 7.1 years (IQR 3.4–10.0 years), CD4 percentage was 9.0% (IQR 3.0–17.0%), and 61.3% were in World Health Organization (WHO) stage 3 or 4. Seventy-four percent were initiated on an NNRTI-based regimen. The death and lost to follow-up rates were 1.3 (95% confidence interval (CI) 1.1–1.6) and 2.2 (95% CI 1.6–2.6)/100 patient-years of follow-up, respectively. At the last clinic visit of 919 children, the median CD4 percentage was 27.0% (IQR 23.0–32.0%) and 80.2% had HIV-RNA <40 copies/ml. WHO stage 1 or 2 at ART initiation was associated with having a viral load <40 copies/ml ($p < 0.002$), and baseline CD4 ≥15% and starting with a three-drug regimen were associated with achieving CD4 ≥25% ($p < 0.001$).
Conclusions: Although most children initiated ART at low CD4 levels, the majority achieved immune reconstitution and long-term virological control. Earlier treatment may improve these outcomes.

1. Introduction

The introduction of highly active antiretroviral therapy (HAART) has improved the outcomes of HIV-infected children and adolescents.[1–5] A long-term follow-up study among perinatally HIV-infected children and adolescents showed that the use of HAART reduced mortality from 7.2 to 0.8/100 person-years between 1994 and 2000, and this remained relatively stable through 2006.[1,2] Studies of antiretroviral therapy (ART) outcomes in resource-limited settings have also shown encouraging clinical outcomes.[3,4,6–8] A study in the Democratic Republic of the Congo demonstrated that HAART reduced the mortality risk in HIV-infected children by 75%.[3] Changes in the causes of death in HIV-infected children and adolescents have also been observed during the HAART era. Deaths due to opportunistic infections have declined, but non-AIDS-defining infections and multi-organ failure have become the major causes of mortality.[2]

In resource-limited settings, there continues to be a major gap in coverage of ART for children compared to adults. It is estimated

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that only 23% of children who need ART receive it compared to 51% of adult counterparts.[9] Furthermore, available information on the long-term outcomes of treatment in children in low- and middle-income countries is limited. The 'Pediatric Progress' database was set up to systematically collect clinical data from four major referral sites in Thailand. As Thailand has been facing the HIV epidemic longer than other Asian countries, and the National Program providing ART has been established since the year 2000, this database affords a unique opportunity to study long-term treatment outcomes in children.

2. Materials and methods

We conducted a pooled analysis of data from the pediatric HIV-infected cohort in the Pediatric Progress database, from four collaborative referral sites in Thailand, including two sites in Bangkok (Siriraj Hospital and The HIV Netherlands Australia Thailand Research Collaboration (HIV-NAT)) and two sites in northern Thailand (Chiangrai Prachanukroh Hospital and Sanpatong Hospital). The inclusion criteria were HIV-infected children and adolescents <18 years of age at study entry who had initiated ART. HIV-infected children and adolescents who were older than 18 years of age at study entry and those who had not initiated ART, or who had an uncertain ART regimen or start date, were excluded. All sites are able to access HIV RNA and CD4 testing. Children were followed clinically every 3 months. CD4 counts and percentages were monitored every 6 months and HIV RNA viral loads (VL) every 12 months. Treatment followed the national guidelines, with the use of non-nucleoside reverse transcriptase inhibitor (NNRTI)-based HAART as the preferred first-line regimen; ART was fully available at no cost to the patient, supported by the Ministry of Public Health. Data were collected prospectively from 2008 until March 2011. Data from before 2008 were retrieved retrospectively from the medical records, back to ART initiation, which was first started in 1996. Baseline CD4 and VL were collected at ART initiation. Baseline CD4 counts and percentages were the measurements closest to ART initiation, as long as this was between 180 days prior to and 14 days after ART initiation. Baseline VL was considered to be the result taken closest to the initiation of ART, within a period of 365 days before and 14 days after ART initiation. The first ART regimen used was

Table 1
Demographic characteristics of 1139 HIV-infected children at ART initiation

Characteristics	<18 months (n = 179)	18–59 months (n = 205)	≥60 months (n = 755)	Overall (n = 1139)	p-Value
Site					<0.001
Siriraj Hospital	136 (76)	88 (42.9)	130 (17.2)	354 (31.1)	
HIV-NAT	21 (11.7)	53 (25.9)	136 (18)	210 (18.4)	
Chiangrai Prachanukroh Hospital	21 (11.7)	61 (29.8)	454 (60.1)	536 (47.1)	
Sanpatong Hospital	1 (0.6)	3 (1.5)	35 (4.6)	39 (3.4)	
Gender					0.187
Female	85 (47.5)	103 (50.2)	411 (54.4)	599 (52.6)	
Age at ARV initiation, median (IQR) years	0.6 (0.4–1)	3.3 (2.3–4.2)	9.1 (7.2–11.1)	7.1 (3.4–10.0)	<0.0001
Mode of transmission					0.587
Mother to child transmission	174 (97.2)	200 (97.6)	727 (96.3)	1101 (96.7)	
Blood transfusion	0 (0)	0 (0)	4 (0.5)	4 (0.4)	
Sexual transmission	0 (0)	0 (0)	3 (0.4)	3 (0.3)	
Sexual abuse	0 (0)	0 (0)	1 (0.1)	1 (0.1)	
Breast feeding	1 (0.6)	1 (0.5)	0 (0)	2 (0.2)	
Unknown	4 (2.2)	4 (2)	20 (2.6)	28 (2.5)	
WHO stage at ARV initiation					<0.001
Stage 1	12 (6.7)	12 (5.9)	86 (11.4)	110 (9.7)	
Stage 2	21 (11.7)	32 (15.6)	176 (23.3)	229 (20.1)	
Stage 3	40 (22.4)	63 (30.7)	161 (21.3)	264 (23.2)	
Stage 4	36 (20.1)	42 (20.5)	197 (26.1)	275 (24.1)	
Unavailable data	70 (39.1)	56 (27.3)	135 (17.9)	261 (22.9)	
Initial ARV regimen					<0.001
Mono/dual NRTIs	111 (62)	62 (30.2)	59 (7.8)	232 (20.4)	
Triple NRTIs	1 (0.6)	1 (0.5)	3 (0.4)	5 (0.4)	
NNRTI-based HAART	37 (20.7)	133 (64.9)	674 (89.3)	844 (74.1)	
PI-based HAART	29 (16.2)	7 (3.4)	11 (1.5)	47 (4.1)	
Other	1 (0.6)	2 (1)	8 (1.1)	11 (1)	
ARV regimen at last clinic visit (n = 919)					<0.001
Mono/dual NRTIs	5 (4.1)	8 (4.9)	11 (1.7)	24 (2.6)	
NNRTI-based HAART	48 (39.7)	95 (57.9)	473 (74.6)	616 (67)	
PI-based HAART	41 (33.9)	39 (23.8)	98 (15.5)	178 (19.4)	
Double-boosted PIs	1 (0.8)	1 (0.6)	8 (1.3)	10 (1.1)	
Triple classes	8 (6.6)	3 (1.8)	5 (0.8)	16 (1.7)	
Third-line regimens[a]	8 (6.6)	7 (4.3)	12 (1.9)	27 (2.9)	
Other	10 (8.3)	11 (6.7)	27 (4.3)	48 (5.2)	
Duration of ARV therapy, median (IQR) years	5.6 (2.2–11.1)	6.6 (3.6–8.8)	5.2 (2.9–7.1)	5.5 (2.9–7.6)	<0.0001
Cause of death					0.002
HIV-related	3 (30)	3 (60)	56 (84)	62 (76)	
Non-HIV-related	2 (20)	1 (20)	6 (9)	9 (11)	
Unknown	5 (50)	1 (20)	5 (7)	11 (13)	

ART, antiretroviral therapy; ARV, antiretroviral; HAART, highly active antiretroviral therapy; IQR, interquartile range; NNRTI, non-nucleoside reverse transcriptase inhibitor; NRTI, nucleoside reverse transcriptase inhibitor; PI, protease inhibitor; WHO, World Health Organization.

[a] Third-line regimens included darunavir, maraviroc, and etravirine-based regimens. Fifteen of 27 children were on third-line regimens because of virological failure, and 11 of these were initially treated with mono or dual NRTI. Two children were participating in clinical trials using these agents. The remaining 10 children had been treated with mono or dual NRTI and after developing resistance had switched to single or double-boosted PI regimens. These children were switched to darunavir because of severe dyslipidaemia. The median duration of ART treatment in these 27 children was 9 years (IQR 5–12 years).