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Delays in fast track antiretroviral therapy initiation and reasons for not starting treatment among eligible children in Eastern Cape, South Africa

Chloe A. Teasdale[a,b], **Katharine A. Yuengling**[a], **Anthony Mutiti**[a], **Stephen Arpadi**[a,b], **Mahlubandile Nxele**[c], **Lungile Pepeta**[c,d], **Mary Mogashoa**[e], **Emilia D. Rivadeneira**[f], **Elaine J. Abrams**[a,b,g]

[a]ICAP at Columbia;

[b]Department of Epidemiology, Mailman School of Public Health, Columbia University, New York, New York, USA;

[c]Port Elizabeth Hospital Complex;

[d]Nelson Mandela University, Faculty of Health Sciences, Port Elizabeth;

[e]US Centers for Disease Control and Prevention, Pretoria, South Africa;

[f]US Centers for Disease Control and Prevention, Atlanta, Georgia;

[g]College of Physicians & Surgeons, Columbia University, New York, New York, USA.

Abstract

We report data from an observational cohort of South African children living with HIV less than 12 years of age eligible for fast track antiretroviral therapy (rapid) initiation. We found that less than half of children eligible for rapid antiretroviral therapy initiation based on immunologic and disease status started treatment within 1 week.

Timely identification of HIV infection in infants and immediate initiation of antiretroviral therapy (ART) are critical for reducing mortality; earlier treatment is associated with a 76% decreased risk of death in infants [1]. Rapid ART initiation for children who were missed through early infant diagnosis programs is also critical for improving survival. The WHO recommends a test and treat approach, regardless of clinical or immunologic status, for children and adults living with HIV [2]. Many high HIV burden countries continue to face challenges with respect to identifying and initiating treatment in all children living with HIV (CLHIV) [3]. Starting in April 2013, the South African National HIV Treatment Guidelines recommended ART for all children aged less than 5 years and for children aged 5–15 years

Correspondence to Chloe A. Teasdale, ICAP-Columbia University, Mailman School of Public Health, Columbia University, 722 W168th Street, Room 1319, New York, NY 10032, USA. Tel: +1 212 304 7920; fax: +1 212 342 1824; ct116@columbia.edu.

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Conflicts of interest

There are no conflicts of interest.

with WHO stage 3 or 4 or $CD4^+$ of 350 cells/μl or less [4]. The guidelines also called for 'fast-track' ART initiation within 7 days of eligibility for children aged less than 12 months and those aged at least 12 months with $CD4^+$ less than 200 cells/μl or $CD4^+$ percentage less than 15%, WHO clinical stage 4 or drug resistant tuberculosis (DRTB). In this analysis, we examined data from an observational pediatric cohort conducted in Eastern Cape, South Africa and report on an early effort to fast-track ART initiation for children.

The *Enhanced Surveillance and two Year Outcomes of Children Enrolled on ART in Public Health Facilities in the Eastern Cape Province, South Africa* (PESS), was an observational cohort study that enrolled ART-naïve CLHIV from birth through 12 years of age at five health facilities in Eastern Cape, South Africa [5]. CLHIV identified as ART-eligible by healthcare workers (HCW) were recruited from 2012 and followed through 2015. Caregivers provided consent, assent was taken for children aged at least 8 years. Enrolled children received routine HIV care at facilities and attended additional quarterly study visits for up to 24 months, which included physical exams, blood specimen collection and abstraction of routine medical record data, including ART start date and reasons for delayed ART initiation. Children missing study visits were tracked through phone calls and home visits. Ethics approval was received from Columbia University, University of Cape Town, East London Hospital Complex Research Ethics Committee, Walter Sisulu University Health Research Ethics Committee and Eastern Cape Department of Health, and was reviewed by the CDC Center for Global Health Associate Director for Science Office.

The current analysis includes CLHIV enrolled in PESS after 1 April 2013 who required fast-track ART initiation (excluding those eligible based on DRTB for which data were not available). Children who attended at least one follow-up study visit are included. Those who died, withdrew, or transferred prior to their first study follow-up visit were excluded. We describe the characteristics of children at the time of study enrollment (which coincided with treatment eligibility), time from enrollment to ART initiation and associations between enrollment characteristics and ART initiation within 7 days. Competing risk estimators were used to assess the cumulative incidence of ART initiation, treating death as the competing risk. Multivariable modified Poisson regression models were fitted to estimate the relative risk of maternal and child characteristics with timely ART initiation adjusted for enrollment characteristics selected *a priori*, including age at enrollment, sex, primary caregiver, maternal age, weight age *z*-score (WAZ), $CD4^+$, and viral load. Models were adjusted for intrasite clustering across the study facilities.

Among 446 CLHIV aged 12 years or less identified by healthcare providers as ART-eligible, 401 caregivers consented for study enrollment, 397 children were enrolled, including 149 (42.1%) enrolled after 1 April 2013 who were eligible for fast-track ART initiation and had at least one follow-up visit. Among the children eligible for fast-track ART initiation, 84 (56.4%) were aged less than 12 months (Table 1). At enrollment, 42.3% of children were hospitalized, and 24.8% had tuberculosis (TB). Mothers were primary caregivers for 73.2% of children and, among 139 (93.3%) mothers alive at enrollment, almost 70% were more than 25 years. At study enrollment, median WAZ was −2.1 [interquartile range (IQR): −3.6 to and −0.5] median viral load was 907 857 copies/ml (IQR: 278 885–2389 465).

Among fast-track eligible children, the cumulative incidence of ART initiation at 1 week was 47.7% [95% confidence interval (CI): 39.4–55.4] and at 1 month was 78.5% (95% CI: 68.1–81.9). Median time to ART initiation among fast-track eligible children was 8 days (IQR: 0–23); 14 (9.4%) started ART more than 90 days after enrollment and two (1.3%) never started. In multivariable analysis, children were less likely to have started ART within 7 days of eligibility if they had their mother as the primary caregiver [adjusted risk ratio (aRR) 0.67; 95% CI: 0.60–0.74] but were more likely to have started if they had a pretreatment viral load more than 100 000 copies/ml (aRR 1.36; 95% CI: 1.02–1.81). Reasons for delayed ART initiation (>90 days) were recorded in the charts of 10 children; three (30%) were delayed because HCWs reported that the caregiver had not completed adherence counseling or had not brought a treatment supporter (adult living in same home), three (30%) children were delayed as a result of HCWs reporting that caregivers had ‘social problems’, two (20%) were delayed as a result of the caregiver not returning to pick up medications, and two (20%) because of TB treatment.

In this cohort of CLHIV aged 12 years or less who were eligible for immediate treatment initiation based on age or immunologic status, less than half started ARTwithin 1 week and a quarter had not started within a month. In multivariable models, children were significantly less likely to start ARTwithin 7 days if they had their mothers as the primary caregiver whereas children with higher pretreatment viral load were more likely to initiate within 7 days. There was little information regarding why children were not immediately started on ART, however available information suggested that most children were delayed based on perceived adherence concerns by HCWs. It is imperative that children, particularly young children and those with advanced disease, initiate treatment as quickly as possible. Our data suggest that, in this early effort to rapidly initiate ART in children at high risk for poor outcomes, greater efforts were needed to ensure that HCWs immediately start treatment in all eligible children. They also suggest a need for strategies to help caregivers of CLHIV attend visits and pick-up medications which could include transport reimbursement and/or extended clinic hours.

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Table 1.

Characteristics at study enrollment among South African children in the Eastern Cape, living with HIV and eligible for fast track antiretroviral treatment initiation[a] (*N* = 149).

	ART initiation within 7 days						
	All		Started ART		Did not start ART		
	N	%	*N*	%	*N*	%	*P* value
	149	100.0	71	47.7	78	52.4	
Age at enrollment, median month (IQR)	9.9 (3.5–71.9)		8.0 (3.2–86.5)		10.3 (4.1–66.6)		0.6771
<12 months	84	56.4	42	59.2	42	53.9	0.7702
1–5 years	28	18.8	11	15.5	17	21.8	
6–12 years	37	24.8	18	25.4	19	24.4	
Age at HIV diagnosis, median months (IQR)	8.0 (2.0–52.0)		6.0 (1.8–52.0)		9.5 (2.0–52.0)		0.7456
< 12 months	87	58.4	42	59.2	45	57.7	0.8486
1–3 years	20	13.5	9	12.7	11	14.1	
>3 years	42	28.2	20	28.2	22	28.3	
Female	66	44.3	31	43.7	35	44.9	0.8820
Child hospitalized at enrollment	63	42.3	23	32.4	40	51.3	0.0198
Child hospitalized ever	89	59.7	39	54.9	50	64.1	0.2923
Child tuberculosis at enrollment	37	24.8	15	21.1	22	28.2	0.3179
Mother alive at enrolment	139	93.3	64	90.1	75	96.2	0.1429
Primary caregiver							
Mother	109	73.2	47	66.2	62	79.5	0.1820
Grandmother	21	14.1	13	18.3	8	10.3	
Other	19	12.8	11	15.5	8	10.3	
Mother >25 years at enrollment (among alive at enrollment)	97	69.8	46	71.9	51	68.0	0.6200
Inside tap in home	82	55.0	37	52.1	45	57.7	0.4941
Electricity in home	134	89.3	66	93.0	68	87.2	0.2417
Enrollment WAZ, median (IQR)	−2.1 (−3.6 to −0.5)		−1.7 (−2.9 to −0.5)		−1.9 (−3.2 to −0.5)		0.6979
<−2	64	48.9	30	44.1	34	54.0	0.5197
−2 to −1	24	18.3	14	20.9	10	15.9	
>−1	43	32.8	24	35.3	19	30.2	

	ART initiation within 7 days						
	All		Started ART		Did not start ART		
	N	%	*N*	%	*N*	%	*P* value
Missing	18	12.1	3	4.2	15	19.2	0.0050
Enrollment viral load, median (IQR)	907 857 (278 8852389 465)		607 380 (337 9562123 455)		1003 575 (264 2552797 207)		0.8655
>1 million	65	47.1	28	42.4	37	51.4	0.2736
100 000–1 million	52	37.7	30	45.5	22	30.6	
10 000–99 999	15	10.9	5	7.6	10	13.9	
<10 000	6	4.4	3	4.6	3	4.2	
Missing	11	7.4	5	7.0	6	7.7	0.8795
Enrollment $CD4^+$ cell count, median (IQR)	478 (230–1284)		467 (152–1367)		486 (268–953)		0.8108
>1000	41	30.4	23	37.7	18	24.3	0.0790
500–1000	24	17.8	6	9.8	18	24.3	
350–499	23	17.0	10	16.4	13	17.6	
200–349	16	11.9	5	8.2	11	14.9	
<200	31	23.0	17	27.9	14	18.9	
Missing	14	9.4	10	14.1	4	5.1	0.0613
Enrollment $CD4^+$%, median (IQR)	12.5 (8.6–21.0)		12.1	(8.5–21.0)	13.1 (8.8–20.7)		0.2033
>40%	9	6.7	4	6.7	5	6.8	0.9832
25–40%	19	14.2	8	13.3	11	14.9	
15–24%	25	18.7	12	20.0	13	17.6	
<15%	81	60.5	36	60.0	45	60.8	
Missing	15	10.1	11	15.5	4	5.1	0.0357
Time to ART initiation days, median (IQR)	8 (0–23)		0 (0–2)		23 (14–56)		
<1 week[a]	47.7 (39.5–55.4)						
<1 month	78.5 (68.1–81.9)						
<3 months	89.3 (83.1–93.3)						

ART, antiretroviral therapy; IQR, interquartile range; WAZ, weight for age *z*-score.

[a]Cumulative incidence of time to ART initiation calculated using competing risk estimators.

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