VIROLOGIC RESPONSE TO ANTIRETROVIRAL THERAPY INITIATED AT ≤ 12 WEEKS OF AGE

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Background

- There have been shifts towards widespread effective prevention of mother-to-child transmission of HIV (PMTCT) coverage. The socio-demographic characteristics and viral response of infants infected despite a high coverage of effective PMTCT programs, may differ from infants infected in previous periods.
- In addition, HIV birth testing implementation in South Africa has allowed for initiation of antiretroviral therapy (ART) in the first few weeks of life.
- Virologic suppression in HIV-infected infants occurs more slowly than in older children, and the response in infants treated within the first few weeks of life in the context of routine care, has not been well described.
- We aim to describe viral suppression during the first 6 months on ART among infants starting treatment aged ≤12 weeks, in 3 different time periods corresponding to PMTCT and infant ART guideline changes.

Methods

- A retrospective cohort analysis of HIV-infected infants who started ART aged ≤12 weeks from 2006-2016 at 9 South African IeDEA-SA sites.
- Infants included had ≥1 viral load (VL) measurement between 3-9 months on ART.
- Viral suppression was defined as as VL <400 copies/ml (cpm) and compared proportions of infants suppressed across ART initiation cohorts: 2006-2009, 2010-2012 and ≥ 2013.
- X^2 and Kruskal-Wallis tests were used to assess differences in infant characteristics across ART initiation cohorts.
- We used logistic regression models to identify determinants of failure to suppress beyond 400 cpm by 6 months on ART.

Results

- Of 777 HIV-infected infants included, 56% were female, median age at ART initiation was 9 weeks (Interquartile range (IQR): 5-11) and decreased with successive ART initiation cohorts.
- Median $\log_{10}$ VL and CD4% were 5.86 (IQR: 4.8-6.4) cpm and 27 (IQR 18.6-37.8) respectively with improvements in most recent ART initiation cohort.
- The proportion of infants virally suppressed by 6 months on ART was 66% in 2006-09, 63% in 2010-12 and 51% in 2013-16 (p=0.002). In a subset of 450 infants with additional VL measured at 12 months (10-15 months) on ART, the proportion suppressed at 12 months decreased from 76% in 2006-09 to 60% in 2013-16 (p=0.001)
- There was no significant difference in the median CD4 percentage at 6 months across the ART initiation cohorts (29% vs. 31%, p=0.325 in 2006-09 vs. 2013-16).
- After adjustment for age, gender and CD4 percentage (Table 2), increasing log viral load and ART initiation ≥ 2013 were associated with a higher odds of viral non-suppression (adjusted Odds Ratio (aOR): 1.46; 95% CI: 1.21-1.75 per 1 log increase in VL and aOR: 2.14 ; 95% CI: 1.37-3.22 for infants starting ART ≥2013 vs in 2006-2009, respectively).

Table 1. Description of the cohort at ART initiation

ART initiation characteristics	Overall N=777	2006-2009 N= 224	2010-2012 N=249	2013-16 N= 304	p-value*
Age (days)	63 (38-79)	70 (56-83)	67 (46-80)	47 (9-75)	<0.001
Female	441 (55.6)	113 (50.4)	148 (59.4)	171 (56.2)	< 0139
CD4 Percentage	581	197	189	195	
	27 (18.6-37.8)	21(14.0-32.5)	27(20.6-37.8)	32 (23.0-42.0)	<0.001
Log viral load	593	196	186	211	
	5.8 (4.6-6.4)	5.8 (5.3-6.4)	6 (54.8-6.6)	5.3 (4.1-6.3)	<0.001
WHO stage III/IV	510	182	147	189	
	308 (60)	154 (76)	84 (57)	70 (37)	<0.001
WAZ	597	208	209	180	
≤ -2	320(53.6)	134 (64.4)	111 (53.1)	75 (41.6)	0.001
>- 2	277 (46.4)	74 (35.5)	98 (46.9)	105 (58.3)	
PMTCT Exposed	777	224	249	304	
Yes	316 (40.7)	92 (41.1)	84 (33.7)	140 (46.1)	0.029
No	317 (40.8)	85 (37.9)	113 (45.3)	119 (39.1)	
Unknown	144 (18.5)	47 (21.0)	52 (20.8)	45 (14.8)	

Proportions are shown as n (%). Continuous variables are reported as median (interquartile range). Missing baseline data for CD4 percentage, weight-for-age Z-score (WAZ) and WHO stage were modelled using multiple imputation.

Table 2. Adjusted associations between time period of ART start and failure to suppress <400 cpm

Characteristics	Unadjusted			Adjusted		
	OR	95% CI	p-value	AOR	95% CI	p-value
Age in weeks	1.39	1.01-1.92	0.042	1.10	0.73-1.65	0.628
Female	0.82	0.67-1.71	0.179	0.75	0.55-1.02	0.073
ART initiation year						
2006-2009	reference			reference		
2010-2012	1.51	1.04-2.18	0.028	1.45	0.96-2.19	0.071
≥ 2013	1.56	1.12-2.27	0.009	2.14	1.37-3.22	0.001
Log viral load	1.2	1.08-1.44	0.002	1.46	1.21-1.75	<0.001
CD4 percentage	0.98	0.97-1.00	0.059	0.99	0.97-1.00	0.208
WHO disease stage						
Stage I/II	reference			reference		
Stage III/IV	1.07	0.78-1.46	0.658	-	-	-
WAZ						
≤-2	reference			reference		
>-2	0.98	0.95-1.01	0.255	-	-	-

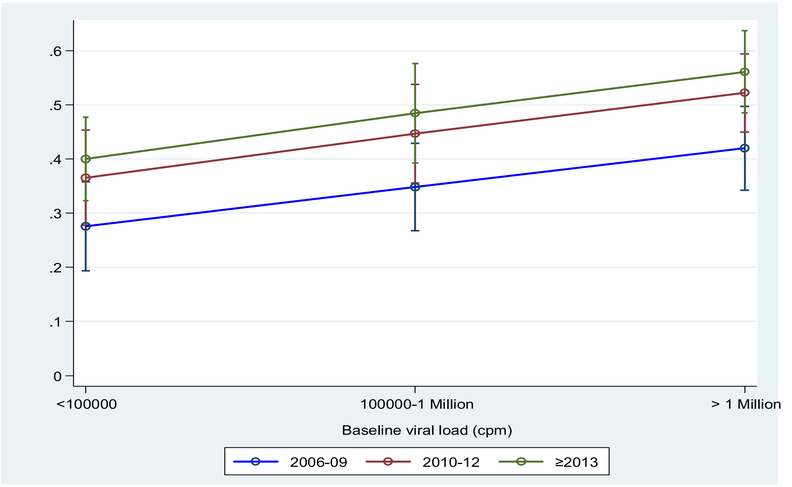


Figure 1. Adjusted predictions of non-suppression (<400 cpm) with 95 % confidence intervals among 777 HIV-infected infants initiating antiretroviral therapy within 12 weeks of age.

Discussion

- Overall, HIV infected infants initiating ART in 2013-16 were twice as likely to not suppress below 400 cpm by 6 months on ART compared to those initiating in 2006-09.
- The odds of not being suppressed by 6 months on ART did not vary significantly by age of ART initiation.
- Poorer virologic suppression in infants who initiated ART ≥ 2013 compared to earlier years is a major concern, especially as infants starting in recent years had higher CD4% and lower VL at ART initiation.
- Poorer virologic outcomes in recent cohorts may be linked to limited antiretroviral formulations for very young infants and additional risk factors such as prematurity, co-morbidities and suboptimal ART adherence, which may be more common in infants infected with HIV despite widespread PMTCT.
- While our study is an important step forward, further research is needed to understand reasons for worse virologic outcomes in recent years.

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