EARLY POSTPARTUM VIREMIA PREDICTS LONG-TERM NON-SUPPRESSION AND INFANT TRANSMISSION

000765

Megan Landes[1,2], Monique van Lettow[1,3], Joep J van Oosterhout[4,5], Erik Schouten[6], Andrew Auld[7], Thokozani Kalua[8], Andreas Jahn[8,9], Beth A Tippett Barr[10]

1. Dignitas International, Zomba, Malawi 2. Department of Family and Community Medicine, University of Toronto, Canada 3. Dalla Lana School of Public Health, University of Toronto, Canada 4. Partners in Hope, Lilongwe, Malawi 5. David Geffen School of Medicine, University of California Los Angeles, USA 6. Management Sciences for Health, Lilongwe, Malawi 7. Centers for Disease Control and Prevention, Lilongwe, Malawi 8. Ministry of Health, Lilongwe, Malawi 9. I-TECH, Department of Global Health, University of Washington, Seattle, USA 10. Centers for Disease Control and Prevention, Kisumu, Kenya

BACKGROUND

Long-term viral load suppression among HIV-positive reproductive-aged women on antiretroviral therapy (ART) is key to eliminating infant HIV transmission. While pregnancy remains an important entry point for the current global 'Treat All' strategy, there is limited information at a population level regarding longitudinal viral load suppression in this sub-cohort of persons on ART. We report trends in postpartum viral load for Malawian women on ART, factors associated with detectable viral load, and associations with cumulative infant HIV transmission and/or death.

METHODS

From 2014-2016, 1-6 months postpartum (PP) HIV-positive mothers were screened and enrolled with their infants in Malawi clinics. At enrollment, 12 and 24 months postpartum, socio-demographic and prevention of mother to child transmission (PMTCT) of HIV indicators were collected. All infants had HIV-1 DNA testing and venous samples determined maternal plasma viral load (<40 copies/ml = 'undetectable'). National PMTCT guidelines were to offer all pregnant and breastfeeding women lifelong ART and standard national VL monitoring was in early implementation across Malawi.

RESULTS

Table 1. Characteristics of HIV-infected mothers enrolled for follow-up to 24 months

		Enrolment 1-6 months post-partum	Annual visit 1 12 months post-partum	Annual visit 2 24 months post-partum
	N	1281	773	596
Region				
North Central Rural		335 (26.2)	186 (24.1)	161 (27.0)
North Central Urban		392 (30.6)	193 (25.0)	131 (22.0)
South Rural		156 (12.2)	123 (15.9)	111 (18.6)
South Urban		398 (31.1)	271 (35.1)	193 (32.4)
Mother's age in years				
<19		79 (6.2)	50 (6.4)	35 (5.9)
20-24		287 (22.4)	145 (18 .8)	102(17.1)
25-29		335 (26.2)	197 (25.5)	152 (25.5)
>30		576 (45.0)	379 (49.0)	305 (51.2)
Missing		4 (0.3)	2 (0.3)	2 (0.3)
Weeks postpartum at enrolment, median (IQR)		8 (6-13)	—	—
Parity				
1		192 (15.0)	108 (14.0)	76 (12.8)
2-3		633 (49.4)	366 (47.3)	275 (46.1)
>4		454 (35.4)	298 (38.6)	244 (40.9)
Missing		2 (0.2)	1 (0.1)	1 (0.2)
Level of Education				
None or primary education		839 (65.5)	492 (63.6)	385 (64.6)
Secondary or post-secondary education		440 (34.3)	280 (36.3)	211 (35.4)
Missing		2 (0.2)	1 (0.1)	—
Maternal HIV status at time of study screening (4-26 weeks post-partum)				
Already known HIV-infected		1208 (94.3)	743 (96.1)	579 (97.1)
Newly diagnosed HIV-infected		73 (5.7)	30 (3.9)	17 (2.9)
Mother's reported disclosure of her HIV status to her partner at each visit				
Yes, partner knows her HIV-positive status		1058 (82.6)	651 (84.2)	502 (84.2)
No, partner does not know her HIV-positive status		143 (11.2)	27 (3.5)	57 (9.6)
No partner		73 (5.7)	89 (11.5)	32 (5.4)
Missing		7 (0.5)	6 (0.8)	5 (0.8)
Maternal ART Initiation[$] (as reported at enrolment)				
Started ART pre-conception		561 (43.8)	354 (45.8)	288 (48.3)
Started ART post-conception (during pregnancy or post-partum)		590 (46.1)	362 (46.8)	278 (46.6)
Not started ART		87 (6.8)	53 (6.9)	29 (4.9)
Missing		43 (3.4)	4 (0.5)	1 (0.2)
Maternal ART status[$]				
On ART		1178 (92.0)	755* (97.7)	590** (99.0)
Not started ART		87 (6.8)	1 (0.1)	
Started but Stopped ART		14 (1.1)	15 (1.9)	6 (1.0)
Missing		2 (0.2)	2 (0.3)	
Time on ART in months (at time of visit) among those on ART, median (IQR)		8.3 (5.2-39.5)	19.2 (15.9-50.4)	30.1 (26.8-61.3)
Time on ART in months (at time of visit) among those on ART				
<3.0		75 (6.4)	3 (0.4)	0
3.1-6.0		275 (23.3)	3 (0.4)	0
6.1-12.0		229 (19.4)	49 (6.5)	4 (0.7)
12.1-18.0		31 (2.6)	238 (31.5)	6 (1.0)
18.1-24.0		39 (3.3)	89 (11.8)	47 (8.0)
>24		345 (29.3)	297 (39.3)	483 (81.9)
Missing		184 (15.6)	76 (10.1)	50 (8.5)
Mothers' Self-reported health status				
Well		1214 (94.8)	746 (96.5)	563 (94.5)
Minor Illness		52 (4.1)	23 (3.0)	17 (2.9)
Major Illness		8 (0.6)	0 (0)	0 (0)
Missing		9 (0.5)	4 (0.5)	16 (2.7)

[$] *Self-reported and verified/amended with clinical records when available*
*including 39 women not (yet) on ART at enrolment of which 24 newly diagnosed at study enrolment
**including 27 women not (yet) on ART at enrolment of which 17 newly diagnosed at study enrolment

Detectable VL in early postpartum signals a significant risk of ongoing viremia to 24 months postpartum with implications for infant HIV transmission, in a setting with limited high VL management.

- The proportion of women on ART achieving undetectable VL (<40 copies/ml) was 77.4% at enrollment, 85.4% at 12 months and 80.2% at 24 months.
- Overall, 86.7% (n=1021/1178) women self-reported optimal adherence (i.e.<2 days missed ART in past month) at enrollment, 91.4% (n=690/755) at 12 months and 91.4% (n=539/590) at 24 months.
- Of 590 women on ART (median 30.1 mos. (IQR 26.8-61.3)), 442 (74.9%) with VL data at all 3 visits were included in further analysis. Among those 17/442 were not (yet) on ART at study enrolment (see Table 2):
  - ***345 (81.8%) women had durable undetectable VL, 16 (3.6%) lost viral load suppression and out of the 81 (18.3%) women with detectable VL at enrolment, 33 (40.7%) had persistent detectable VL.***
  - ***Cumulative incidence of detectable VLs over 24 months was higher among women with detectable VL at enrollment (n=40/81; 49.4%) compared to those with undetectable VL (n=13/361; 3.6%); p<0.001.***

Table 2. Women with 3 Viral Load observations n=442 on ART at enrolment n=425 not on ART at enrolment n=17 (including 10 newly diagnosed)

Women on ART from Study Enrolment n=425

Enrolment		12 month visit		24 month visit	
<40	359	<40	353	<40	343
				40-1000	5
				>1000	5
		40-1000	3	<40	2
				40-1000	1
				>1000	0
		>1000	3	<40	1
				40-1000	1
				>1000	1
40-1000	27	<40	18	<40	15
				40-1000	3
				>1000	0
		40-1000	4	<40	0
				40-1000	2
				>1000	2
		>1000	5	<40	1
				40-1000	0
				>1000	4
>1000	39	<40	12	<40	9
				40-1000	0
				>1000	3
		40-1000	3	<40	0
				40-1000	1
				>1000	2
		>1000	24	<40	3
				40-1000	1
				>1000	20

Women NOT on ART at study enrolment n=17

Enrolment		12 month visit		24 month visit	
<40	2*	<40	2	<40	2
				40-1000	
				>1000	
		40-1000		<40	
				40-1000	
				>1000	
		>1000		<40	
				40-1000	
				>1000	
>1000	15**	<40	12	<40	11
				40-1000	1
				>1000	0
		40-1000	1	<40	
				40-1000	
				>1000	1
		>1000	2	<40	2
				40-1000	
				>1000	

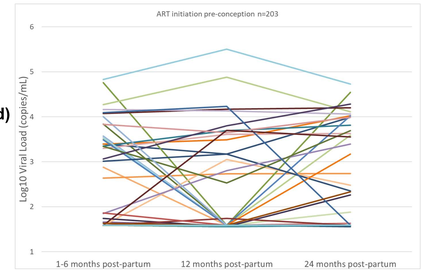
*2 known HIV-positive mothers (1 reported to have never started and 1 having stopped ART)

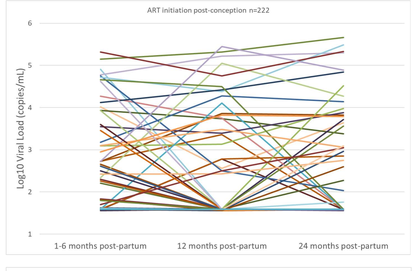
** incl 10 newly diagnosed not yet on ART and 5 known HIV-positive mothers (3 reported to have never started and 2 having stopped ART)

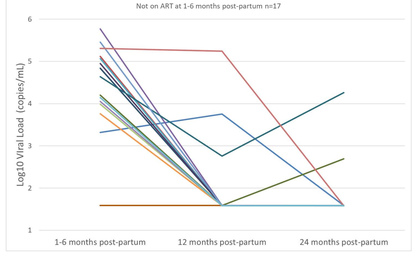
Table 3. Factors associated with detectable viral load (VL >40) at 24 months postpartum among women on ART and having complete VL data (N=442)

			VI>40 vs those with VL<40 around infant age 24 months			
			Univariate (unadjusted)		Multivariable (adjusted)	
	n/n	%	OR (95%CI)	*p-value*	aOR (95%CI)[#]	*p-value*
Total	**53/442**	**12.0**				
Mother's age in years						NS
<24	11/104	10.6	0.8 (0.4-1.9)	0.60		
>25	42/336	12.5	ref			
Missing	0/2					
Parity, %						NS
1-2	15/141	10.6	0.8 (0.4-1.5)	0.55		
3+	38/301	2.6	ref			
Level of Education						NS
None or primary education	29/272	10.7	0.7 (0.4-1.3)	0.28		
Secondary or post-secondary education	24/170	14.1	ref			
Mother's reported disclosure of her HIV status to her partner at any time during the study						NS
Yes, partner knows her HIV-positive status	43/400	12.0	ref			
No partner throughout study period or mother never disclosed during study period	5/42	12.2	1.0 (0.4-2.6)	0.98		
Maternal ART Initiation						NS
Pre-conception (started ART before last pregnancy)	24/203	11.8	ref			
Post-conception (started ART during last pregnancy or post-partum)	27/222	12.2	1.0 (0.6-1.9)	0.91		
New infections/not on ART at enrolment	2/17	11.8	0.99 (0.2-4.6)	0.99		
Combined Self-reported adherence at 12 and 24 month (among those on ART)						NS
Fully optimal* adherence over time	37/358	10.3	ref			
At least one sub-optimal** adherence measure	16/83	19.3	2.1 (1.1-3.9)	0.03		
Missing (data available for 1 visit only)	0/1	0.0				
Cumulative detectable VLs						
0 previous detectable (>40) VL	10/355	2.8	ref			
1 previous detectable (>40) VL	10/48	20.8	9.1 (3.6-23.2)	0.0001	9.0 (3.5-23.0)	0.0001
2 previous detectable (>40) VL	33/39	84.6	189.8 (64.9-555.0)	0.0001	226.4 (73.0-701.8)	0.0001

[#] Adjusted for all variables in the model. All variables were simultaneously entered in the logistic regression model and tested for removal through backward stepwise selection.
* Reported to have missed ART 0 or 1 day in the last month in all visits (2 or 3).
** Reported to have missed ART 2 or more days in the last month in 1 or more previous visits.







- In multivariable analysis, adjusted odds ratios (aORs) for detectable VL at 24 months were 9.0 among women with 1 prior detectable VL (95%CI 3.5-23.0, p<0.0001) and 226.4 for women with 2 prior detectable VLs (95%CI 73.0-701.8, p<0.0001) (adjusted for age, parity, education, partner disclosure, time on ART and adherence).
- Women who had 3 visits with undetectable VL (N=345) had no HIV infant transmissions, and 2 infant deaths (0.6% combined outcome). Women with at least one detectable viral load (n=64) had 7 HIV infant transmissions (10.9%) and 1 infant death (1.6%). Women with 3 visits with detectable VL at each (N=33) had the highest rate of adverse outcomes (15.2%) with 4 infant HIV transmissions (12.1%) and 1 death (3.0%).

CONCLUSIONS

Detectable VL in early PP signals a risk of ongoing PP viremia with major implications for infant HIV transmission, in a setting with limited high VL management.

Limitations include LTFU, yet this effect likely underestimates the true incidence of detectable VL over time. These findings suggest differentiated VL monitoring and targeted adherence support may be required during pregnancy and breastfeeding.

Author contact: megan.landes@utoronto.ca

The Malawi Ministry of Health in collaboration with the Centers for Disease Control and Prevention (CDC) Malawi funded and oversaw this study.