

Changes in HIV-1 Proviral DNA in Women With HIV From Antepartum Through 48 Weeks Postpartum in the IMPAACT P1078 Study.

Grace M. Ahimbisibwe¹, Yanling Huo², Lisa Aaron², Joseph Szewczyk³, Adit Dhummakupt³, Damayanti Yengkhom⁴, Aaron A.R. Tobian³, Avy Violari⁵, Mark Cotton⁶, Amita Gupta³, Adriana Weinberg^{4*}, Philippa Musoke^{1,7*}, Deborah Persaud^{3*}

*Equal contributors

¹Makerere University-Johns Hopkins University (MU-JHU) Research Collaboration, ²Center for Biostatistics in AIDS Research, Harvard T.H. Chan School of Public Health, Boston, MA, USA, ³Johns Hopkins University School of Medicine, Baltimore, MD, USA, ⁴University of Colorado School of Medicine, Anschutz Medical Campus, Aurora, CO, USA, ⁵Perinatal HIV Research Unit, University of Witwatersrand, Johannesburg, South Africa, ⁶Family Center for Research with Ubuntu, Department of Paediatrics & Child Health, Stellenbosch University, Tygerberg, South Africa, ⁷Department of Paediatrics and Child Health, Makerere University College of Health Sciences, Kampala, Uganda

BACKGROUND

Of 40.8 million people living with HIV in 2024, 53% were female. Effective antiretroviral therapy decreases viral replication, HIV-associated morbidity and mortality but does not eliminate the HIV reservoir. Most HIV reservoir research has been conducted in nonpregnant women or in high-income countries where HIV mainly affects males with subtype B HIV infection. Little is known about the dynamics of intact and defective proviruses in pregnant women with HIV (WWH). We present a longitudinal analysis of intact and defective HIV-1 proviral loads for a small fraction of WWH from antepartum through week 48 postpartum.

Amongst all pregnant women with HIV, very stable pools of infected cells are maintained antepartum until 48 weeks postpartum. Slightly lower frequencies of all proviral species are seen with virologic suppression.

METHODS

- This study utilized available PBMC specimens collected at antepartum (N=24), 12 (N=23) and 48 (N=15) weeks postpartum from IGRA-negative South African women in IMPAACT P1078.
- P1078 randomised WWH in the 2nd or 3rd trimester of pregnancy and evaluated the safety of starting immediate (antepartum) versus deferred (postpartum) Isoniazid Preventive Therapy in high-TB settings.
- Using a subtype C-specific Intact Proviral DNA Assay, total, intact and defective proviral HIV-1 DNA were quantified in copies per million PBMCs (cpm).
- Concentrations below the lower limit of detection (LLoD) were imputed as half the LLoD.
- Proviral HIV-1 DNA was described using medians, interquartile ranges and by virologic suppression status.

RESULTS

- Twenty-three women had at least one result; 14 contributed all 3 timepoints and 9 contributed 2 timepoints. One participant had no results due to Env amplification failure.
- Median age at study entry was 30.5 (IQR:28-35) years. Median CD4 count was 458.5 (IQR:348.0-646.5) cells/mm3, and 92% had WHO stage 1 HIV. HIV-1 RNA viral load at entry was < 50 copies/mL in 63% of participants. Median duration on antiretrovirals prior to study entry was 10.5 (IQR: 2.5-48.5) weeks (Table 1).
- The antepartum, week 12 and week 48 postpartum medians (IQR) total proviral HIV-1 DNA were 2.3 (2.0-2.7), 2.3 (2.0-2.5) and 2.4 (2.0-2.6) log10 cpm respectively (Figure1). Intact proviral HIV-1 DNA levels were 1.5 (1.0-2.0), 1.5 (1.2-1.9) and 1.6 (1.4-1.9) log10 cpm respectively (Figure1). In participants with HIV-1 plasma RNA <50 copies/mL throughout the study, total proviral HIV-1 DNA was 2.0 (1.9-2.3), 2.1 (1.8-2.3) and 2.1 (1.9-2.4) log10 cpm, and for intact provirus 1.3 (0.9-1.7), 1.4 (1.1-1.6) and 1.4 (1.0-1.6) log10 cpm (Table 2).

TABLE 1. Baseline Characteristics

Characteristic		Total (N=24)
Age (years)	Median (Q1, Q3)	30.5 (28.0, 35.0)
Gestational age category (weeks)	14 - < 24	12 (50%)
	24 - 34	12 (50%)
HIV-1 RNA viral load (copies/mL) at entry	< 50	15 (63%)
	50 - < 200	3 (13%)
	≥ 200	6 (25%)
Time on ARVs prior to entry (weeks)	Median (Q1, Q3)	10.5 (2.5, 48.5)

ACKNOWLEDGMENTS

The IMPAACT P1078/TB APPRISE Protocol Team gratefully acknowledges the dedication and commitment of the 956 mother-infant pairs, their communities, and CAB representatives, without whom this study would not have been possible. The authors also wish to acknowledge the IMPAACT P1078/TB APPRISE Protocol team, NIAID, NICHD, and NIMH, and the thirteen IMPAACT sites and staff.

FIGURE 1. Box plots of log10 proviral HIV-1 DNA by study visit, among all WWH

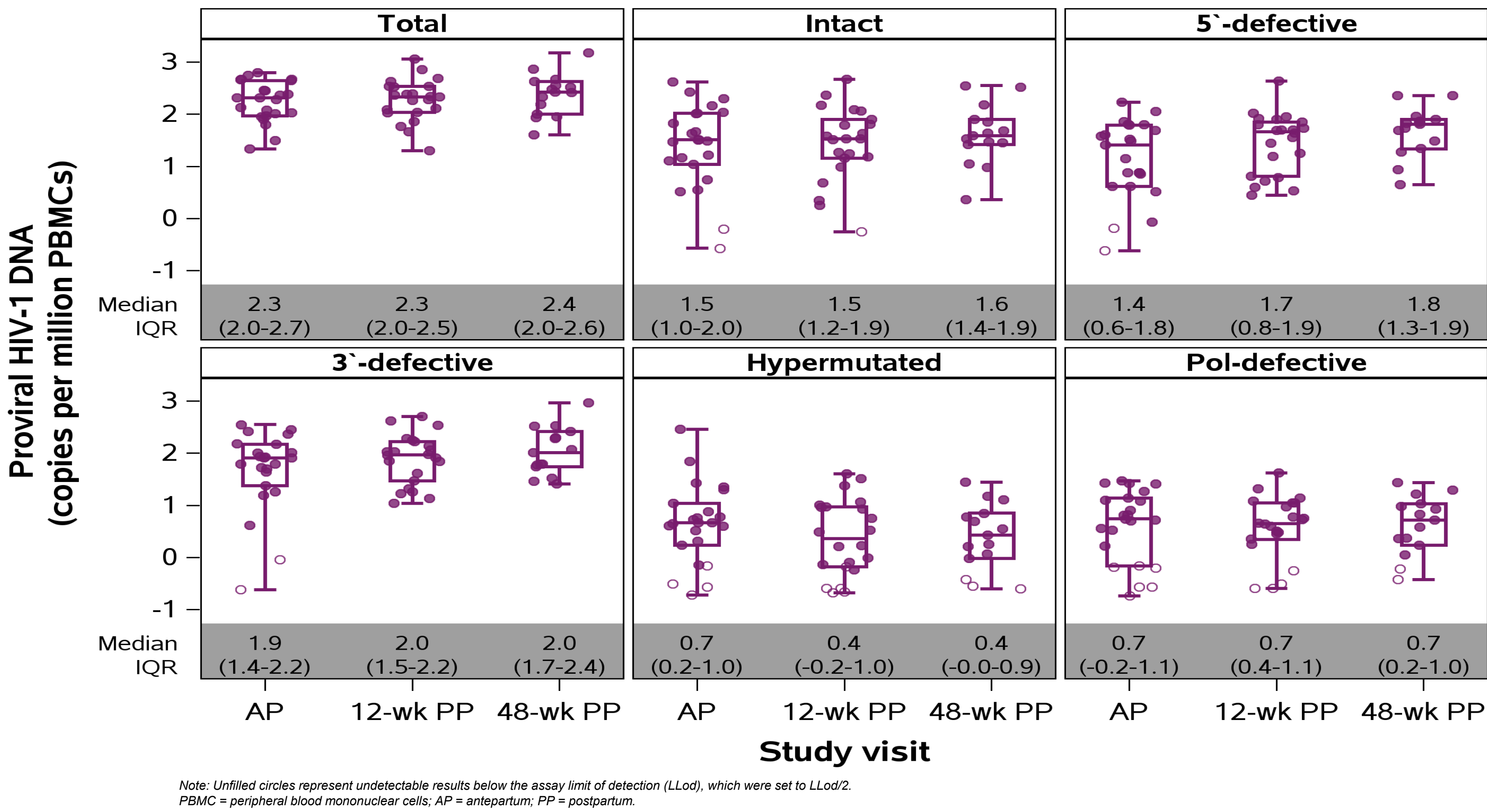


TABLE 2. Proviral HIV-1 DNA by virologic suppression* status, by study visit

	Antepartum (N=23)			12 weeks postpartum (N=22)			48 weeks postpartum (N=15)		
Proviral HIV-1 DNA	wVLS (N=12)	woVLS (N=11)	P-value**	wVLS (N=12)	woVLS (N=10)	P-value**	wVLS (N=8)	woVLS (N=7)	P-value**
Total	2.0 (1.9,2.3)	2.7 (2.3,2.7)	0.003	2.1 (1.8,2.3)	2.5 (2.3,2.6)	0.01	2.1 (1.9,2.4)	2.6 (2.5,2.9)	0.02
Intact	1.3 (0.9,1.7)	1.8 (1.2,2.3)	0.15	1.4 (1.1,1.6)	2.0 (1.3,2.2)	0.04	1.4 (1.0,1.6)	1.9 (1.5,2.5)	0.02
% intact of total	21.2 (9.2,47.6)	27.2 (8.7,42.4)	0.95	15.9 (8.9,26.9)	26.5 (7.6,40.9)	0.49	14.6 (7.5,27.5)	21.7 (8.5,47.7)	0.27
5'-defective	1.3 (0.9,1.7)	1.4 (0.6,1.8)	0.88	1.4 (0.8,1.8)	1.7 (1.5,2.0)	0.17	1.5 (1.1,1.9)	1.8 (1.7,2.4)	0.12
3'-defective	1.8 (1.2,1.9)	2.0 (1.7,2.4)	0.04	1.8 (1.3,2.0)	2.1 (1.9,2.3)	0.09	1.8 (1.6,2.2)	2.3 (1.8,2.5)	0.16
Hypermutated	0.4 (-0.3,0.7)	0.9 (0.7,1.4)	0.01	-0.1 (-0.6,0.8)	0.8 (0.2,1.0)	0.12	0.1 (-0.2,0.3)	0.8 (0.6,1.2)	0.07
Pol-defective	0.4 (-0.2,0.8)	1.1 (0.7,1.4)	0.06	0.5 (0.0,0.7)	0.9 (0.6,1.1)	0.08	0.4 (-0.1,1.0)	0.8 (0.4,1.3)	0.12

Median (IQR): Log 10 transformed
wVLS – With VL suppression; woVLS – Without VL suppression; * VL suppression was defined as HIV-1 RNA viral load < 50 copies/mL across all visits.
** P-value from Wilcoxon rank-sum test for continuous variable.

CONCLUSIONS

- Median total and intact HIV-1 proviral DNA concentrations tended to remain stable from antepartum to postpartum and were slightly lower among those with virologic suppression.
- 3'-defective proviruses were present at higher concentrations than 5'-defective proviruses at all 3 timepoints, and increased from antepartum to 12, and 48 weeks postpartum. Pol defective proviruses were unchanged and hypermutated proviruses decreased postpartum.
- The findings provide insights into the dynamics of total and intact HIV-1 proviruses during pregnancy and postpartum in WWH.
- Additional research with larger sample sizes is warranted.

