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Changes in bone mineral during and after lactation in Ugandan women on Option B+ ART

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BACKGROUND

- ART (antiretroviral treatment) in persons living with HIV (PWH) is associated with bone loss and increased risk of fracture, but data are limited in pregnant and lactating women when physiological bone mineral mobilization is also occurring.
- This research investigated changes in areal bone mineral density (aBMD) in breastfeeding Ugandan women with HIV (WWH) initiated on lifelong ART in pregnancy compared to HIV-negative counterparts (REF).

METHODS

- Two groups of pregnant Ugandan mothers planning to breastfeed, 95 WWH (on Option B+ ART [TDF-3TC-EFV], previously ART naïve) and 96 REF took part.
- Measurements were made postpartum at 2 (L2), 14 (L14), and 26 (L26) weeks of lactation, and at 14 weeks post-lactation when neither pregnant nor lactating (NPNL).
- Lumbar spine (LS), total hip (TH), femoral neck (FN) and whole body-less-head (WBLH) aBMD was measured by DXA.

RESULTS

- Median Maternal age was 24.5 (IQR 21.1, 26.9) yrs, and not significantly different between the groups (Table 1).
- WWH had lower body weight and shorter duration of breastfeeding (Table 1).
- Both groups mobilized bone mineral all the skeletal sites during lactation (Figure 1).
- However, WWH compared to REF had greater decreases in TH, FN and WBLH aBMD during lactation (Figure 1).
- Both groups had higher LS aBMD at NPNL relative to L2 (Figure 1).
- Hip and WBLH aBMD had returned to L2 values in REF but not in WWH by NPNL (Figure 1).
- Adjusting for potential confounders (parity, breastfeeding practices, weight and DMPA) did not attenuate the results.

Ugandan women on triple ART (TDF-based) had accentuated mobilization of hip and whole body bone mineral during lactation, and slower skeletal recovery at 3 months post-lactation, compared to HIV-negative counterparts.

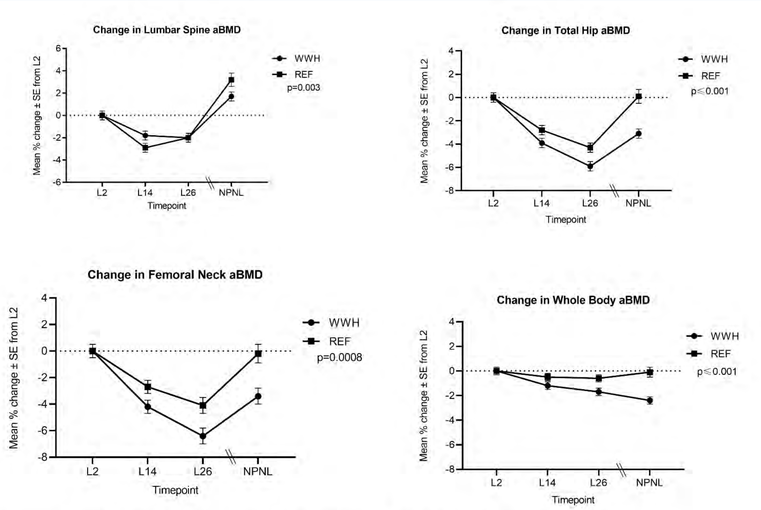


Figure 1: Percent changes in aBMD during and after lactation in HIV^{ve} and HIV^{-ve} Ugandan women
Data are mean percent changes (%Δ) ± standard errors (SE). LS = lumbar spine, TH= total hip, WBLH = whole body-less-head, aBMD = areal bone mineral density (g/cm2), WWH = women with HIV initiated on lifelong triple ART during pregnancy (TDF-3TC-EFV, previously ART naïve), REF = women without HIV (reference group, ART naïve), L2, L14, L26 = 2, 14 and 26 weeks postpartum, respectively, NPNL = Neither Pregnant Nor Lactating. NPNL measurement was scheduled at 14 weeks after lactation. Results were obtained from Scheffé post hoc tests for group*visit (time point) interaction terms in hierarchical repeated measures ANOVA models that included subject (nested by group), group, visit, and group*visit interaction in DataDesk 6.3.1 software. All variables were transformed into natural logarithms (loge) and multiplied by 100 before data analysis. P-values are for comparison of overall patterns of changes between the groups (WWH vs. REF). Adjusting for parity, age, body size, breastfeeding practices, duration of breastfeeding, use of depo-provera and resumption of menses did not attenuate the results.

Table 1: Summary of participant characteristics and medical history at L2, L14, L26 and NPNL

	L2		L14		L26		NPNL	
	WWH (n=84)	REF (n=78)	WWH (n=83)	REF (n=81)	WWH (n=69)	REF (n=72)	WWH (n=67)	REF (n=32)
Weeks postpartum	2.2±0.5	2.1±0.4	14.3±0.6	14.2±0.8	26.5±0.9	26.7±1.0	65.1±14.1[a]	81.1±18.4
Age (years)	23.5(21.2,27.2)	23.0(20.7,27.0)	23.4(21.3,27.1)	23.2(20.7,27.0)	23.5(21.5,27.2)	23.0(20.8,26.9)	23.9(21.7,27.3)	22.9(20.7,27.4)
Parity	2 (1, 3)	1 (1, 2)	2 (1, 3)	1 (1, 2)	2 (1, 3)	1 (1, 2)	2 (1, 3)	1 (1, 2)
Primiparous, %	36.9 [c]	53.8	36.1[c]	55.6	37.7 [c]	54.2	32.8 [c]	53.1
Weeks on ART	17.6±5.5	-	29.5±5.1	-	42.0±5.7	-	80.4±15.5	-
CD_4 cell count	400 (301, 516)	-	407 (290, 528)	-	487 (343, 674)	-	471 (339, 687)	-
% pills taken[1]	99.3±2.0	-	99.7±1.6	-	99.4±3.3	-	99.2±3.9	-
EBF, %	82.1 [a]	59.7	89.2 [a, 2]	65.4 [2]	88.4 [a]	45.8	-	-
BF duration, weeks	2.2±0.5	2.1±0.4	14.1±0.6	14.2±0.8	26.5±0.9	26.7±1.0	47.8±13.4[a]	65.6±18.1
Resumed menses, %	-	-	39.8	34.6	56.5	51.4	-	-
Current DMPA, %	-	-	30.1 [b]	13.6	34.7	21.7	55.8	43.5
Prior DMPA, %	41.5[b]	19.5	38.3 [b]	18.8	35.3	21.4	43.9 [b]	16.1

Values are means±standard deviations, medians (25 percentiles, 75 percentiles), or percentage (%) of participants reporting "yes").
L2, L14, L26 = 2, 14 and 26 weeks postpartum, respectively; NPNL= measurement made at 14 weeks post-lactation when women were neither pregnant nor lactating; WWH = women with HIV initiated on lifelong triple ART during pregnancy (TDF-3TC-EFV, previously ART naïve), REF = women without HIV (reference group, ART naïve); ART= antiretroviral therapy; CD_4 cell count = cells/cm^3; BF =breastfeeding; EBF = exclusive breastfeeding; DMPA= depot medroxyprogesterone acetate
[1] Mean % adherence to ART based on the pill count method used in routine clinical care = 100*[number of pills taken/number of pills dispensed for the duration].
[2] Proportions are higher than L2 because some babies received pre-lacteal feeds at L2 but were exclusively breastfed at L14.
[a,b,c] P value for differences between the groups obtained from chi-square tests and t-tests in DataDesk 6.3.1 software: [a] p≤0.001, [b] p≤0.01, [c] p≤0.05 .

CONCLUSION

- These data show accentuated mobilization of hip and WBLH bone mineral during lactation, and slower skeletal recovery post-lactation in Ugandan WWH initiated on Option B+ ART in pregnancy (TDF-based) compared to REF.
- Clinical implication of these findings are unclear at this stage.
- Studies are ongoing to understand the mechanisms and long term consequences for bone health and growth of the child.

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