LOW BONE DENSITY ACCRUAL AND INCREASED INFLAMMATION AMONG ZIMBABWEAN ADOLESCENTS WITH PERINATAL HIV

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BACKGROUND

- Peripubertal children living with HIV (CWH) experience **lower bone density and muscle strength** compared to children without HIV (CWOH)[1-3]
- Poor musculoskeletal development **increases risk of fracture, adult-onset osteoporosis and sarcopenia**[4]
- **HIV-associated chronic inflammation** is known to increase risk of chronic disease and may be a mechanism behind poor musculoskeletal health[5]
- **Research gaps:**
  - Limited data investigating the effect of HIV on bone density accrual during puberty
  - The contribution of HIV-associated inflammation via immune-skeletal pathways on bone and muscle health is unknown

OBJECTIVE

To investigate bone density accrual and musculoskeletal-relevant inflammatory biomarkers during puberty among CWH compared to CWOH

METHODS

Participants were 8 to 16 years old CWH from public-sector HIV clinics and CWOH from nearby schools in Harare, Zimbabwe

Perinatally acquired HIV on ART for ≥2 years

Recruited 2018-2019 and followed-up one year later

Bone measurements: Height-adjusted total body less-head bone mineral content (TBLH-BMC) and size-adjusted lumbar spine bone mineral apparent density (LS-BMAD) measured by dual X-ray absorptiometry (DXA). Z-scores calculated.

Muscle measurements: Grip strength using hand-held Jamar dynamometer, standing long jump distance, DXA-measured lean mass

Blood sample: Collected at first visit. Plasma analysed for CRP, sCD14, IL18, IL17α, IL6 , IL10, IFNγ, TNFα using Luminex.

Statistical analysis: Separate adjusted linear regression models for males and females. Change in (Δ) bone density accounted for the number of days passed between visits. Factorial analysis of mixed data was used to reduce inflammatory biomarker data.

References: *(1)* Rukuni R *et al.* Effect of HIV infection on growth and bone density in peripubertal children in the era of antiretroviral therapy: a cross-sectional study in Zimbabwe. Lancet Child Adol Health. 2021;5:569–81. *(2)* Gregson CL *et al.* Perinatal HIV infection is associated with deficits in muscle function in children and adolescents: a cross-sectional study in Zimbabwe. AIDS. 2023. *(3)* Shen Y *et al*. Persistently lower bone mass and bone turnover among South African children living with well controlled HIV. AIDS. 2021;35:2137–47. *(4)* Frigati L *et al.* Chronic comorbidities in children and adolescents with perinatally acquired HIV infection in sub-Saharan Africa in the era of antiretroviral therapy. Lancet Child Adol Health. 2020;4:688–98. *(5)* Tuttle CSL *et al.* Markers of inflammation and their association with muscle strength and mass: A systematic review and meta-analysis. Ageing Res Rev. 2020. 1;64.

RESULTS: Longitudinal bone density outcomes

244 CWH (mean age 13.0 years (SD 2.3), 199 (48.8%) girls
248 uninfected children (12.9 years (SD 2.4), 126 (50.8%) girls)

Mean difference (MD) (95% CI) in change in DXA Z-scores between CWH and CWOH

		Unadjusted		Adjusted[1]	
		MD (95% CI)	p	MD (95% CI)	p
Male (n=236)	ΔLS-BMAD-Z	**-0.17 (-0.29, -0.04)**	**0.008**	**-0.18 (-0.30, -0.06)**	**0.003**
	ΔTBLH-BMC-Z	**-0.16 (-0.32, -0.00)**	**0.046**	**-0.21 (-0.36, -0.06)**	**0.007**
Female (n=235)	ΔLS-BMAD-Z	0.001 (-0.12, 0.12)	0.988	0.02 (-0.09, 0.13)	0.714
	ΔTBLH-BMC-Z	0.001 (-0.13, 0.14)	0.994	0.02 (-0.11, 0.16)	0.742

1. Adjusted for age, pubertal stage and baseline Z-score

RESULTS: HIV-associated inflammation

Biomarkers were reduced to two components

- Dimension 1 associated with **IL18, CRP, CD14, TNFα** (26.5% of data variance)
- Dimension 2 associated with **IFNγ, IL17α, IL6 and IL10** (17.6% of data variance)

Linear regression for the association of HIV status with inflammation

	Dimension	Univariable		Multivariable[1]	
		β (95% CI)	p	β (95% CI)	p
Male (n=275)	1	**0.81 (0.47, 1.15)**	**<0.001**	**0.80 (0.45, 1.15)**	**<0.001**
	2	-0.34 (-0.63, -0.06)	0.019	-0.27 (-0.57, 0.03)	0.075
Female (n=283)	1	**0.80 (0.47, 1.12)**	**<0.001**	**0.63 (0.27, 0.98)**	**0.001**
	2	-0.03 (-0.31, 0.25)	0.836	0.02 (-0.29, 0.32)	0.909

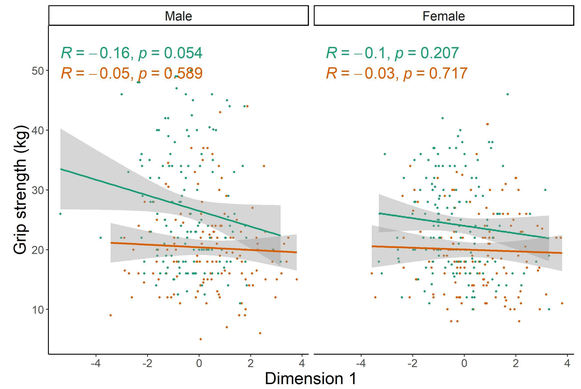
1. Adjusted for age and pubertal stage

Linear regression for the association of bone outcomes with inflammation

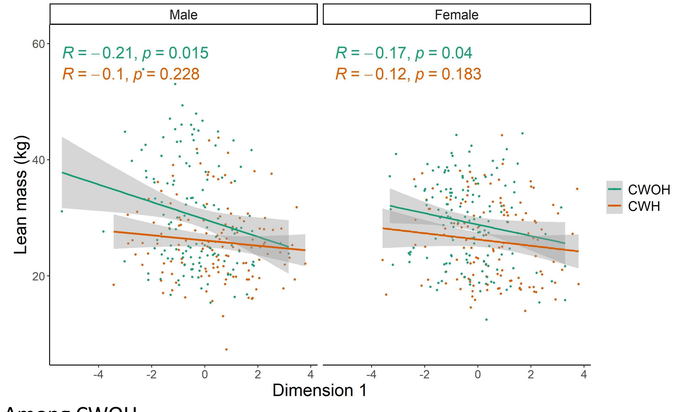
	Dimension	LS-BMAD Z-score		TBLH-BMC Z-score	
		β (95% CI)[1]	p	β (95% CI)[1]	p
Male (N=136)	1	-0.09 (-0.22, 0.05)	0.225	-0.02 (-0.13, 0.09)	0.694
	2	0.02 (-0.19, 0.22)	0.881	0.04 (-0.13, 0.20)	0.673
Female (N=134)	1	**0.19 (0.05, 0.32)**	**0.008**	**0.13 (-0.00, 0.25)**	**0.055**
	2	0.07 (-0.11, 0.24)	0.438	0.01 (-0.16, 0.17)	0.938

1. Adjusted for age and pubertal stage, TBLH-fat mass

RESULTS: Inflammation and bone and muscle outcomes



Scatter plots of the correlation between dimension 1 and grip strength (kg) and lean mass (kg)



Among CWOH,

- Increased inflammation correlated with lower grip strength and lean mass
- No association between inflammation and bone outcomes

CONCLUSIONS

- Males living with HIV gained less LS-BMAD and TBLH-BMC over one year compared to males without HIV
- Among males and females, living with HIV is associated with increased musculoskeletal-relevant inflammatory biomarkers
- Compared to CWOH, CWH have an altered response to increased inflammation:
  - positively associated with bone density outcomes among females with HIV
  - no correlation with grip strength nor lean mass

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