Comparing telomere length between children who were and were not exposed to HIV in Kenya

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Background

- Telomere length (TL) is an important biomarker of aging.[1]
- TL shortens from cell division, inflammation, and oxidative stress.[2]
- Children who were HIV exposed and uninfected (CHEU) may experience higher levels of oxidative stress and inflammation compared to children who are HIV unexposed (CHUU).[3]
- Childhood is a time of increased telomere attrition[4] and childhood TL correlates with TL later in life.[5]
- Shorter TL is associated with lower neurodevelopmental scores,[6-8] increased susceptibility to infection,[9] and age-related disease.[10-13]
- There is mixed evidence indicating that CHEU may have shorter[14] or similar[15-16] TL compared to CHUU.

Objective: To compare telomere length (TL) between children who are HIV exposed and uninfected (CHEU) and children who are HIV unexposed and uninfected (CHUU)

Methods

- **Parent study:** HOPE study enrolled 1,000 CHEU and 1,000 CHUU at 6 weeks and followed through 36 months of age
- **Population:** 250 CHEU and 250 CHUU enrolled in HOPE and were retained through 24 months from 6 clinics in Nairobi and Western Kenya
- **Design:** Prospective cohort study
- **Laboratory methods:** TL was measured from dried blood spots using a modified version[17] of the monochrome multiplex qPCR assay[18]
- **Primary outcome:** Relative infant TL reported as the ratio of the amount of telomeric DNA (T) to the single copy gene (S) z-score at the 6-week clinic visit
- **Statistical methods:**
  - Linear mixed effects models with clinic as a random effect.
  - Adjusted for infant age at sample collection, infant sex, maternal age, paternal age, and maternal education.

The analysis plan was pre-registered prior to availability of TL data.

Table 1. Characteristics of CHEU and CHUU with TL at 6 weeks

	n(%) or Median (IQR)	
	CHEU N=250	CHUU N=250
Age at sample collection (weeks)	6.6 (6.0, 7.9)	6.6 (6.0, 7.6)
Female (REF: Male)	130 (52%)	125 (50%)
Birth weight (kg)	3.2 (3.0, 3.5)	3.3 (3.0, 3.6)
Preterm birth (<37 weeks gestation)	7 (2.8%)	7 (2.8%)
Exclusively breastfed at 6 weeks	246 (99%)	238 (95%)
Maternal age (years)	31 (28, 36)	26 (23, 30)
Paternal age (years)	37 (32, 42)	31 (28, 35)
Maternal years of education	8 (8, 12)	12 (9, 12)
Moderate-to-severe food insecurity	63 (25%)	24 (10%)

Infant HIV exposure was not associated with telomere length at 6 weeks of age.

Results

- There were no significant differences between CHEU and CHUU in age at sample collection, sex, birth weight, or preterm birth (Table 1).
- Compared to CHUU, CHEU were more frequently exclusively breastfed and had older parents, mothers with fewer years of education, and households with food insecurity (Table 1).
- Most mothers with HIV were on ART prior to and during pregnancy (88% and 99%, respectively).
  - During pregnancy, 76% of mothers of CHEU were on dolutegravir-based regimens.
- Child HIV exposure was not significantly associated with TL in the simple or adjusted models (Figure 2).

Figure 1. Comparing mean TL z-score between CHUU and CHEU

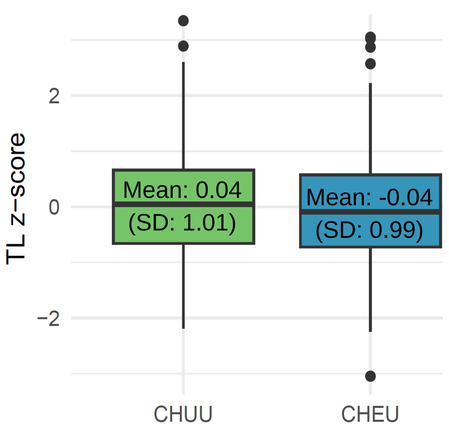
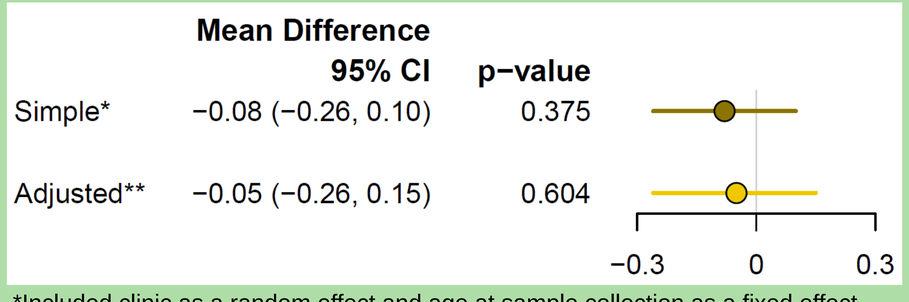


Figure 2. Simple and adjusted models comparing TL between CHEU and CHUU



*Included clinic as a random effect and age at sample collection as a fixed effect
**In addition to simple model, adjusted for sex, maternal age, paternal age, years of maternal education

Conclusions

- In this large cohort, there was no significant difference in 6-week TL between CHEU and CHUU.
- Mothers with HIV were on optimized ART regimens during pregnancy, which could explain why no significant differences in TL were found in this study.
- There is evidence that TL is associated with age-related health outcomes. Further comparison of early TL decline between CHEU and CHUU is warranted.

Additional Key Information

- Future planned analyses in the HOPE study:
  - Compare rate of TL decline from 6 weeks to 24 months between CHEU and CHUU.
  - Determine whether maternal ART regimen or viral load influences child TL among CHEU.
  - Determine the association between early TL and TL decline on neurodevelopmental outcomes of CHEU and CHUU.
  - Assess environmental and disease predictors of TL.

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