PREDICTORS OF NEURODEVELOPMENT IN HIV-EXPOSED UNINFECTED INFANTS

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BACKGROUND

- >1 million HIV-exposed uninfected (HEU) children are born annually in sub-Saharan Africa.
- Mixed evidence indicates increased risk of neurodevelopmental delay, hospitalization, and mortality in HEU children compared to HIV-unexposed uninfected (HUU) children.

OBJECTIVES

- To compare neurodevelopment scores between HEU and HUU infants.
- Among HEU infants, identify ART factors associated with improved neurodevelopment.

Source: Adobe Stock

METHODS

Study Population:

- HEU and HUU infants (aged 4-10 weeks) and their mothers were recruited during routine postnatal care at 6 clinics in Kenya between March-October 2021.

Outcome: Infant neurodevelopment scores

- The Malawi Developmental Assessment Tool (MDAT) scored social, language, fine motor, and gross motor domains.
- Raw scores were the number of items passed per domain (at this young age, ~2 items per domain could be tested).
- Assessments were conducted by trained Kenyan study nurses and routinely reviewed using a standard rubric.
- Multivariate regression models assessed associations with infant HIV/ART exposures, adjusting for *a priori* confounders.

RESULTS

FIGURE 1. Characteristics comparing HEU and HUU

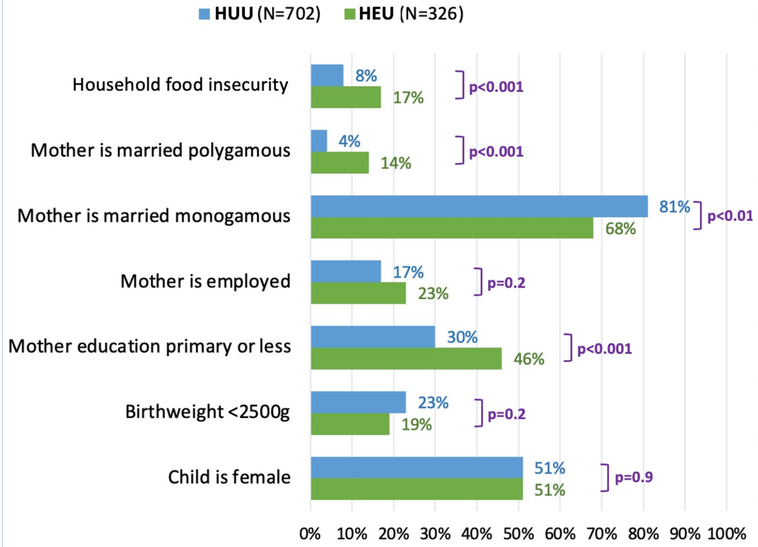

TABLE 1. ART characteristics among HEU

ART Characteristic	N = 326
Child ARV regimen	
AZT + NVP combination	159 (50%)
NVP alone	157 (50%)
Child is currently taking cotrimoxazole	166 (51%)
Maternal ART started pre-conception	277 (87%)
Maternal ART was DTG-based	187 (63%)
Maternal duration on ART (months)	50 (13, 82)

COMPARING HEU vs. HUU:

HEU and HUU infants had comparable neurodevelopment scores at 6 weeks.

AMONG HEU INFANTS:

- Longer maternal ART duration and infant AZT+NVP regimens were associated with higher neurodevelopment scores.
- Maternal viral suppression and dolutegravir-based regimens were not associated with neurodevelopmental differences.

TABLE 2. Comparing raw MDAT neurodevelopment scores between HEU and HUU infants at age 6 weeks, and ART characteristics among HEU (Coeff or PR [95% CI])

Neurodevelopmental Domain:	Social	*p*	Language	*p*	Fine Motor	*p*	Gross Motor	*p*
HEU vs. HUU infants [a]								
HEU (ref: HUU)	-0.10 [-0.23, 0.03]	0.12	0.06 [-0.04, 0.17]	0.23	0.03 [-0.12, 0.18]	0.72	-0.05 [-0.25, 0.15]	0.64
Among HEU [b]								
Child is currently receiving AZT+NVP ART regimen (ref: NVP-alone)	**0.30 [0.09, 0.50]**	**<0.01**	-0.05 [-0.22, 0.12]	0.54	0.14 [-0.23, 0.52]	0.45	**0.37 [0.02, 0.72]**	**0.04**
Maternal ART duration (months)	**0.01 [0.00, 0.01]**	**0.02**	**0.00 [0.00, 0.01]**	**0.04**	0.00 [-0.00, 0.01]	0.21	-0.00 [-0.00, 0.00]	0.70

[a] Multivariate linear regression models adjusted for infant age and sex, and maternal education and marital status.
[b] Multivariate linear regression models adjusted for infant age and sex. Cofactors included in the analysis but were not significant or shown: maternal ART start timing or viral suppression.

Locally sourced items from the MDAT kit (blocks and peg board) used to assess fine motor in older infants. Source: Felix Otieno

CONCLUSIONS

- In this HEU cohort with high frequency of maternal viral suppression and DTG use, neurodevelopment was comparable to HUU infants.
- The mechanisms underlying improved neurodevelopment with longer maternal ART duration and infant combination regimens are unclear.
- Limitation: Determinants of neurodevelopment are difficult to discern at just 6 weeks of age, so longitudinal evaluations will be conducted.

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