Insulin-like Growth Factors and Stunting in African Infants Exposed to HIV and Uninfected

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Background

- About 16 million children are perinatally exposed to HIV and uninfected (CHEU) worldwide (UNAIDS 2024).
- Studies show that they are at increased risk for decreased growth velocity/ stunting through 24 months of age and older when compared to children not perinatally exposed to HIV/ART.
- Stunting is associated with poor birth outcomes, high morbidity, decreased early childhood survival and poorer quality of life in adulthood.
- Key question: Are lower serum concentrations of insulin-like growth factors (IGFs) associated with stunting in CHEU?

Stunting in children defined as length-for-age z-scores (LAZ)< -2 SD below the WHO child growth standards median

Methods

- P1084s:a nested, comparative sub study (within a large VTP trial, IMPAACT 1077) of maternal and infant bone, renal and pediatric growth outcomes of CHEU whose mothers were randomized to TDF-ART, ZDV-ART or ZDV alone during pregnancy.
- We randomly selected 213 infant participants with at least one stored serum sample from Uganda, Malawi and S. Africa and conducted IGF assays on these serum samples at birth, 26 and/or 74 weeks of age.
- Log binomial models estimated risk ratios for stunting.
- Adjusted linear regression models estimated the correlation between LAZ-scores and IGF levels.

Infant demographics in this study at birth

Maternal AP randomization arm		ZDV alone (N=67)	ZDV ART (N=72)	TDF ART (N=74)	All Infants (N=213)
Sex	Male	35 (52%)	32 (44%)	34 (46%)	**101 (47%)**
	Female	32 (48%)	40 (56%)	40 (54%)	112 (53%)
Gestational age at birth (weeks)	Median (Q1, Q3)	38 (38, 40)	38 (38, 40)	38 (37, 40)	38 (38, 40)
Weight (grams)	Median (Q1, Q3)	3,000 (2,780, 3,390)	2,890 (2,600, 3,000)	2,910 (2,600, 3,200)	**2,905** (2,600, 3,200)
WHO weight-for-age z-score	Median (Q1, Q3)	-1 (-1, 0)	-1 (-2, -0)	-1 (-2, -0)	**-1** (-1, -0)
Length (cm)	Median (Q1, Q3)	49 (46, 50)	48 (46, 50)	48 (46, 49)	**48** (46, 50)
WHO length-for-age z-score (LAZ)	Median (Q1, Q3)	-1 (-2, 0)	-1 (-2, -0)	-1 (-2, -0)	**-1** (-2, -0)

Higher IGF-1 levels at birth linked to a lower risk of stunting at week 26.

Growth Factor[1]	Visit Week	Risk of stunting at each visit with growth factor concentration (per log_{10} increase) at birth (Analysis 1)		Cross-sectional association between Infant length-for-age z (LAZ)-score and growth factor concentration (per log_{10} increase) at each visit (Analysis 2)	
		n	Relative Risk (95% CI); p-value	n	Adjusted[2] Coefficient (95% CI); p-value
IGF-1 (log_{10} ng/mL)	0	164	0.80 (0.39, 1.65); 0.55	164	0.21 (-0.32, 0.73); 0.44
	26	133	**0.40 (0.19, 0.86); 0.018**[3]	179	**1.19 (0.62, 1.75); < 0.001**
	74	136	0.63 (0.36, 1.09); 0.10[3]	174	**1.60 (1.15, 2.04); < 0.001**
IGFBP-1 (log_{10} ng/mL)	0	137	0.69 (0.39, 1.24); 0.21	137	0.42 (-0.09, 0.93); 0.11
	26	116	1.32 (0.54, 3.22); 0.55	179	**-0.78 (-1.41, -0.16); 0.014**
	74	117	1.54 (0.76, 3.12); 0.23	174	**-0.62 (-1.21, -0.02); 0.042**
IGFBP-3 (log_{10} ng/mL)	0	53	5.16 (0.06, 480.20); 0.48	53	1.04 (-0.75, 2.83); 0.25
	26	48	1.14 (0.03, 47.05); 0.95	178	**1.81 (0.92, 2.71); < 0.001**
	74	43	1.66 (0.11, 24.19); 0.71	173	**2.08 (1.26, 2.91); < 0.001**

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[1] Priority of growth factor measurement was 1) IGF-1; 2) IGFBP-1; 3) IGFBP-3

[2] Adjusted for treatment, entry CD4, WHO stage, age, time between entry and delivery, breastfeeding duration censored at analysis week and gestational age at birth.

[3] Similar estimates were observed for adjusted model, other adjusted models did not converge

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Conclusion

- This study showed that growth factor concentrations were significantly associated with the LAZ-scores at 26 weeks and 74 weeks.
- Only modest associations between IGF-1 levels at birth and future stunting were shown in this population.
- Future research addressing other possible biologic mechanisms resulting in stunting is needed.
- Identifying and addressing the causes of stunting in CHEU may improve their survival, health and quality of life.