Metabolic Complications in Children HIV Exposed Uninfected in the Pediatric HIV AIDS Cohort Study (PHACS)

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Sahera Dirajlal-Fargo[1], Alicia Jaramillo-Underwood[2], Kunjal Patel[2], Ellen G. Chadwick[1], Mitchell E, Geffner[3], Haleigh Civiletto[4], Alexandria DiPerna[4], Russell B Van Dyke[5], Paige L. Williams[2], Jennifer Jao[1], and Denise Jacobson[2] for the Pediatric HIV/AIDS Cohort Study

[1]Ann & Robert H Lurie Children's Hospital, Chicago, IL, USA, [2]Harvard School of Public Health, Boston, MA, USA, [3]Children's Hospital Los Angeles, Los Angeles, CA, USA, [4]Frontiers Science Foundation, Amherst, NY, USA [5]Tulane University, New Orleans, LA, USA.

BACKGROUND

- Despite avoiding HIV infection, CHEU have shown higher morbidity and mortality than HIV-unexposed children, and emerging evidence suggests potential metabolic effects from *in utero* HIV/ART exposure.
- Metabolic disturbances have been reported in CHEU, though findings across studies remain limited and inconsistent.
- This study aims to characterize metabolic outcomes in CHEU, leveraging fasting metabolic laboratory testing performed from childhood through adolescence.

METHODS

- **Study setting**: PHACS Surveillance Monitoring for ART Toxicities (SMARTT) Study enrolled CHEU in the United States and Puerto Rico within 1 week of birth
- **Inclusion criteria for this analysis**
  - Participants enrolled in SMARTT who met the protocol-defined metabolic trigger (Body Mass Index >95th percentile)
  - At least one fasting metabolic laboratory assay performed within 6 months of the trigger

Statistical analysis:

- In this analysis, follow-up began at 32 months, when children were first evaluated for meeting the BMI trigger, and ended on the date meeting the trigger or at the latest visit.
- We calculated the incidence density of meeting the trigger as the number of participants who met the trigger divided by the number of person-years (PY) at risk.
- Weighted prevalence was estimated after modeling the probability of having any fasting metabolic testing among those meeting the trigger and accounts for potential selection bias due to missing metabolic lab results

Despite averting HIV infection, children who are HIV exposed uninfected and with a high BMI have evidence of cardiometabolic risk factors.

RESULTS

- Of 1669 CHEU enrolled between 2007-2016, 421 (25.2%) met the trigger of BMI >95% at age ≥32 months, among these, 342 had at least one fasting metabolic assessment performed (Table 1).
- Crude and weighted prevalences of metabolic abnormalities among CHEU who met the metabolic trigger are summarized in the Table 2.

Table 1: Baseline characteristics of CHEU who met the BMI trigger and had any metabolic assay

	N=342
Sex at birth (female)	169 (49%)
Black race	205 (60%)
Age (years)	4.3 (1.7)
BMI (kg/m^2)	
Obese (<95th-99th %)	178 (52%)
Maternal Factors	
Age (years)*	33.7 (6)
Black race	193 (56%)
Pre-pregnancy BMI ≥30	149 (44%)
CD4 cell count (≥500)**	167 (49%)
Viral load (<200 c/mL)**	255 (75%)
ART regimen	
PI-based	262 (77%)
INSTI-based	11 (35)

**When child met BMI trigger*
***Prior to delivery*

Table 2: Crude and weighted prevalence of metabolic abnormalities among children exposed to HIV but uninfected with Body Mass Index>95th percentile

Metabolic abnormality	Crude prevalence (95% CI)	Weighted prevalence (95% CI)
High Total Cholesterol (≥200 mg/dL)	6.0% (2.0-13.3%)	5.4% (2.6-8.2%)
High LDL Cholesterol (≥130 mg/dL)	7.1% (2.7-14.9%)	4.0% (1.6-6.5%)
Low HDL Cholesterol (<40 mg/dL)	9.5% (4.2-17.9%)	11.8% (7.8-15.9%)
High Triglycerides (≥ 150 mg/dL)	7.1% (2.7-14.9%)	3.8% (1.5-6.2%)
Dyslipidemia (any of above)	23.8% (15.2-34.3%)	18.6% (13.8-23.4%)
Insulin resistance (HOMA-IR >2.5)	21.1% (12.5-31.9%)	16.8% (12.0-21.6%)

Insulin resistance was assessed using HOMA-IR: [fasting insulin (µU/mL) × fasting glucose (mmol/L)] / 22.535.
Weighted prevalence was estimated after modeling the probability of having any fasting metabolic lab test among those meeting the trigger based on sex at birth, Black race, Hispanic ethnicity, household income, BMI category, age when met trigger (maternal and child), and highest maternal education level.
Laboratory tests were collected within 6 months of meeting the trigger of BMI>95%

CONCLUSIONS

- A substantial proportion of CHEU with high BMI exhibit early cardiometabolic disturbances
- This underscores the need for ongoing monitoring and a deeper understanding of how *in utero* HIV/ART exposure and early-life factors shape long-term metabolic risk.

ACKNOWLEDGMENT

The Pediatric HIV/AIDS Cohort Study (PHACS) network was supported by the Eunice Kennedy Shriver National Institute of Child Health & Human Development (NICHD), and other NIH institutes through grant P01HD103133 to the Harvard T.H. Chan School of Public Health.
We honor the memory of Dr. Denise Jacobson, a valued colleague, mentor and friend, whose guidance and enthusiasm shaped not only this project but all who worked with her.

PLAIN LANGUAGE SUMMARY

Among children who were exposed to HIV during pregnancy but not infected, many who showed early signs of metabolic concerns were found to have cholesterol or blood sugar abnormalities.