Obesity and Metabolic Comorbidities in Young Adults With Perinatal HIV Exposure Without Infection

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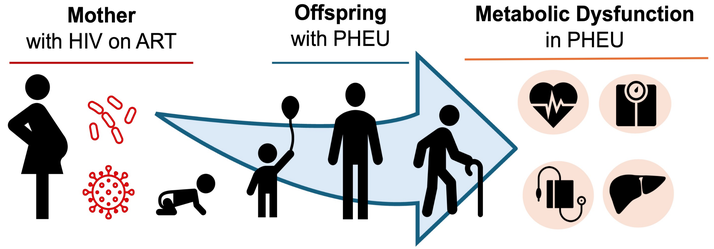
BACKGROUND

- Prenatal antiretroviral therapy (ART) has reduced the vertical transmission rate of HIV to <1%.
- A rising number of individuals with **perinatal HIV exposure without infection (PHEU)** has emerged, now surpassing 20 million globally.
- Infants and children with PHEU experience impaired linear growth, mitochondrial dysfunction, immune activation, and metabolic abnormalities compared to unexposed peers.
- Long-term sequelae of perinatal HIV/ART exposure into adulthood remain largely unknown.

CENTRAL HYPOTHESIS

A perturbed intrauterine environment in HIV influences fetal development to confer an increased susceptibility to obesity and metabolic dysregulation among individuals with PHEU later in life.

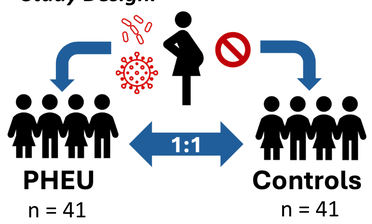
Central Hypothesis.



STUDY DESIGN AND METHODS

- **HIV HEREDITY** is a prospective observational study that enrolled young adults with PHEU (18-35 years) and young adult controls without HIV exposure or infection.
- Young adults with PHEU were matched 1:1 with controls.
- Mothers and young adults were both enrolled and interviewed.
- Prenatal records were accessed when available.
- Endpoints included BMI, measures of body composition, glycemic indices, blood pressure, lipids, and liver fat and stiffness.

Study Design.



Matched 1:1 on ≥4 of 6 criteria: ***Young adult:*** age, sex, race/ethnicity; ***Maternal:*** education, substance use disorder; ***Shared:*** breastfeeding.

Study Procedures.

Visit 1: Mothers & Young Adults
Prenatal and young adult medical histories, HIV test, surveys

Visit 2: Young Adults Only
Anthropometrics, whole-body DXA, serum and plasma samples, Fibroscan®, oral glucose tolerance test, surveys

RESULTS

Young Adult and Maternal Characteristics by PHEU Status.

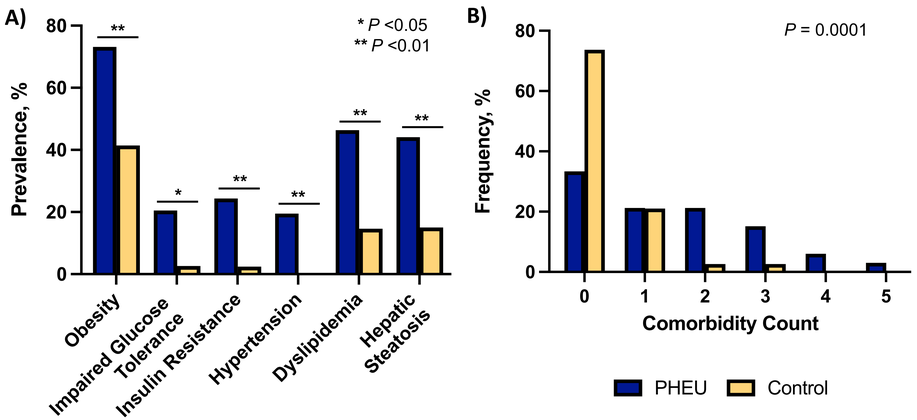
Matching Variables	PHEU (n = 41)	Controls (n = 41)
Young adult – Age, years	24.2 ± 4.8	24.2 ± 4.7
Young adult – Male, n (%)	19 (46)	19 (46)
Young adult – Race/ethnicity, n (%)		
White	10 (24)	16 (39)
Black	16 (39)	12 (29)
More than one race	4 (10)	1 (2)
Other	0	1 (2)
Hispanic/Latinx	11 (27)	11 (27)
Maternal – College, n (%)	10 (24)	16 (39)
Maternal – Substance use disorder, n (%)	21 (51)	10 (24)
Breastfed, n (%)	1 (2)	6 (15)

Prenatal Maternal Factors	PHEU (n = 41)	Controls (n = 41)
Age at delivery, years	29.6 ± 6.0	27.5 ± 6.6
BMI, kg/m^2	29 ± 7	28 ± 7
Parity	2.4 ± 1.4	1.9 ± 1.2
Cesarean section, n (%)	12 (29)	16 (39)
Prenatal tobacco use, n (%)	16 (39)	7 (17)
HIV duration, years	4.4 ± 4.9	
ART duration, years	2.3 ± 3.5	
Prenatal ART, n (%)		
NRTI use	30 (77)	
NNRTI use	5 (13)	
PI	13 (33)	
CD4 count, cells/mm^3	508 ± 249	
HIV viral load <400 copies/mL, n (%)	14 (78)	

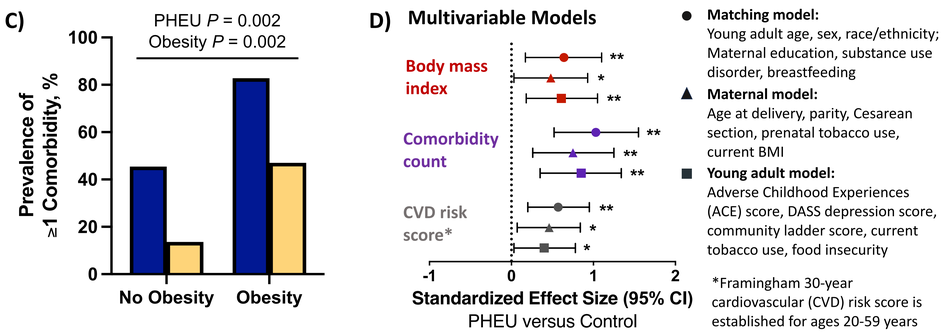
Abbreviations: ART, antiretroviral therapy; BMI, body mass index; NNRTI, Non-nucleoside reverse transcriptase inhibitor; NRTI, nucleoside reverse transcriptase inhibitor; PHEU, perinatal HIV exposure without infection; PI, protease inhibitor. Data are presented as n (%) or mean ± standard deviation.

Obesity and Metabolic Comorbidities in Young Adults with PHEU vs. Controls.

Young Adults with PHEU have a greater burden of obesity and metabolic comorbidities.



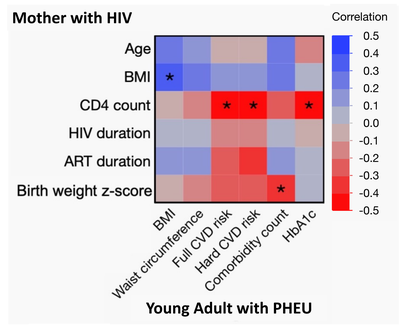
Higher burden of metabolic disease with PHEU C) occurs irrespective of obesity and D) persists in multivariable models adjusting for maternal and young adult factors.

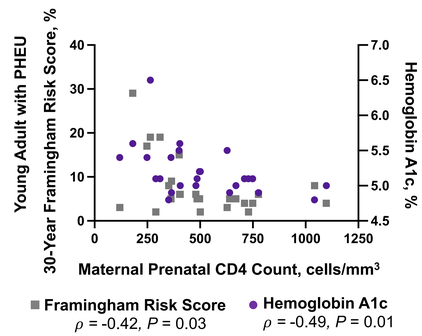


Chi-square tests (A), Student t-test (B), and linear mixed effect models (C, D) were performed. Asterisks (*) denote P <0.05, (**) denote P<0.01.

Correlates of Cardiometabolic Outcomes in Young Adults with PHEU.

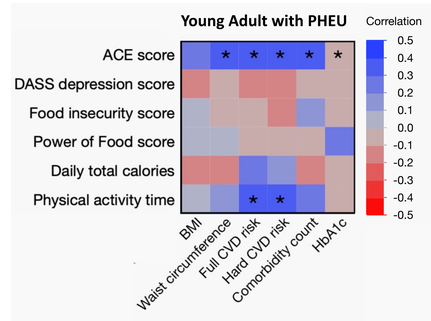
Maternal Prenatal Characteristics (PHEU Group Only)

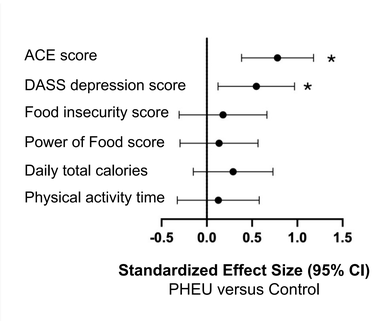




Within the PHEU group, Spearman correlation coefficients and P-values were calculated, including to derive heatmaps. Asterisks (*) denote P<0.05.

Young Adult Characteristics (PHEU Group Only)





Within the PHEU group, Spearman correlation coefficients and P-values were calculated to derive heatmaps. Linear mixed effects models were used to calculate effect sizes between groups for standardized variables. Asterisks (*) denote P <0.05.

Abbreviations: ACE, Adverse Childhood Experiences; ART, antiretroviral therapy; BMI, body mass index; DASS, Depression Anxiety Stress Scales; PHEU, perinatal HIV exposure without infection.

CONCLUSIONS

- Perinatal HIV exposure may play a critical role in shaping adult cardiometabolic disease risk.
- In the oldest-aged cohort studied to date, young adults with PHEU had a greater burden of obesity and metabolic comorbidities, even among individuals without obesity.
- Maternal CD4 count during pregnancy was inversely associated with multiple cardiometabolic endpoints in young adults with PHEU, which may suggest a potential role of maternal immune dysregulation during pregnancy in the pathogenesis of disease.
- Future epigenetic and proteomic analyses of HIV HEREDITY data will further elucidate potential mechanisms of metabolic disease risk among individuals with perinatal HIV exposure.

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