METABOLIC OUTCOMES IN OBESE HIV-EXPOSED UNINFECTED CHILDREN: COMPARISON WITH NHANES

POSTER #874

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BACKGROUND

Metabolic perturbations related to obesity in HIV-exposed uninfected (HEU) children may differ from that in the general obese pediatric population due to *in utero* HIV/antiretroviral (ARV) exposure.

OBJECTIVES

To assess whether obese HEU youth are at increased risk for cardiometabolic risk factors such as hypertension (HTN), dyslipidemia, and insulin resistance compared to a matched group of HIV-unexposed youth in the general United States (U.S.) pediatric population.

METHODS

STUDY POPULATION: HEU children enrolled in the Surveillance Monitoring of ART Toxicities (SMARTT) sub-study of the Pediatric HIV/AIDS Cohort Study (PHACS) constituted the study population, while children who participated in the 2005, 2007, 2009 or 2011 National Health and Nutrition Examination Survey (NHANES) study constituted the comparison population. Because NHANES obtains metabolic measures only within certain age groups, 3 analytic samples were created: 1) TC and HDL (≥6 year), 2) systolic and diastolic BP (≥8 year), and 3) LDL, TG, and HOMA (≥12 year). For each group, up to 3 NHANES youth were matched to each SMARTT participant by age, sex, and race.

EXCLUSION CRITERIA: See Figure for Population Derivation

PRIMARY OUTCOMES: Binary outcomes included-

- **Systolic and diastolic blood pressure (BP) z score ≥90%ile for age, sex, and height**
- **Total cholesterol (TC) >200 mg/dL**
- **High-density lipoprotein-C (HDL) <35 mg/dL**
- **Low-density lipoprotein-C (LDL) >130 mg/dL**
- **Triglycerides (TG) >150 mg/dL**
- **Homeostatic Model Assessment-Insulin Resistance (HOMA) >4**
- **All outcomes were also evaluated as continuous outcomes.**

STATISTICAL ANALYSIS: Modified Poisson regression models were fit for binary outcomes to quantify the prevalence ratio (PR) of each outcome as a function of cohort

TABLE 1. CHARACTERISTICS OF CHILDREN BY COHORT STUDY

BLOOD PRESSURE OUTCOME ANALYTIC SUBGROUP

Characteristic		Total (n=1096)	Study: SMARTT (n=304)	Study: NHANES (n=792)	*p*-Value
Age (yr)		11 (9, 14)	11 (9, 13)	11 (9, 14)	0.03
Black Non-Hispanic		628 (57%)	187 (62%)	441 (56%)	0.09
Female		568 (52%)	153 (50%)	415 (52%)	0.54
Annual household income ($)	< 20,000	369 (37%)	148 (67%)	221 (29%)	< 0.01
	20,000 - 50,000	419 (42%)	62 (28%)	357 (46%)	
	> 50,000	201 (20%)	11 (5%)	190 (25%)	
BMI-Z		2.07 (1.86, 2.35)	2.07 (1.87, 2.40)	2.07 (1.85, 2.33)	0.17
In utero ART regimen	No ARVs	--	11 (4%)	--	
	Non-combination ART	--	49 (16%)	--	
	≥ 3 NRTIs	--	35 (12%)	--	
	NNRTI-based ART	--	36 (12%)	--	
	PI-based ART	--	158 (52%)	--	
	≥ 3 ARV classes	--	1 (0%)	--	
	Missing	--	14 (4%)	--	
In utero exposure to AZT, d4T, ddI, or ddC		--	261 (86%)	--	

HDL AND TC OUTCOME ANALYTIC SUBGROUP

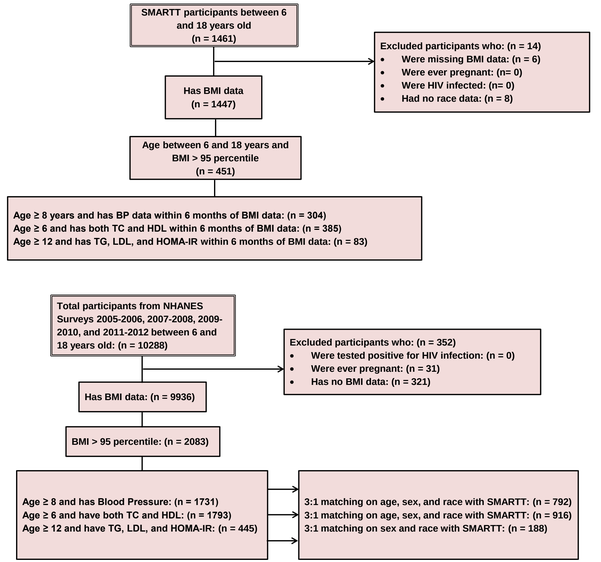
Characteristic		Total (n=1301)	Study: SMARTT (n=385)	Study: NHANES (n=916)	*p*-Value
Age (yr)		10 (8, 13)	9 (7, 11)	10 (8, 14)	<0.01
Black Non-Hispanic		657 (50%)	224 (58%)	433 (47%)	<0.01
Female		696 (53%)	196 (51%)	500 (55%)	0.25
Annual household income ($)	< 20,000	450 (38%)	189 (63%)	261 (30%)	<0.01
	20,000 - 50,000	511 (43%)	96 (32%)	415 (47%)	
	> 50,000	219 (19%)	16 (5%)	203 (23%)	
BMIZ		2.08 (1.87, 2.38)	2.08 (1.88, 2.41)	2.09 (1.86, 2.38)	0.53
In utero ART Regimen	No ARVs in pregnancy	--	13 (3%)	--	
	Non-combination ART	--	61 (16%)	--	
	≥ 3 NRTIs	--	39 (10%)	--	
	NNRTI-based ART	--	41 (10%)	--	
	PI-based ART	--	210 (55%)	--	
	INSTI-based ART	--	3 (1%)	--	
	≥ 3 ARV classes	--	2 (1%)	--	
	Missing	--	16 (4%)	--	
In utero exposure to AZT, d4T, ddI, or ddC		--	335 (87%)	--	

LDL, TG, and HOMA-IR ANALYTIC SUBGROUP

Characteristic		Total (n=271)	Study: SMARTT (n=83)	Study: NHANES (n=188)	*p*-Value
Age (yr)		15 (13, 16)	14 (13, 15)	15 (13, 17)	<0.01
Black Non-Hispanic		179 (66%)	60 (72%)	119 (63%)	0.17
Female		151 (56%)	53 (64%)	98 (52%)	0.09
Annual household income ($)	< 20,000	97 (40%)	37 (60%)	60 (33%)	<0.01
	20,000 - 50,000	96 (40%)	20 (32%)	76 (42%)	
	> 50,000	50 (21%)	5 (8%)	45 (25%)	
BMIZ		2.09 (1.85, 2.43)	2.09 (1.86, 2.43)	2.09 (1.85, 2.42)	0.87
In utero ART Regimen	No ARVs	--	6 (7%)	--	
	non-combination ART	--	31 (38%)	--	
	≥ 3 NRTIs	--	5 (6%)	--	
	NNRTI-based ART	--	12 (15%)	--	
	PI-based ART	--	26 (31%)	--	
	≥ 3 ARV classes	--	1 (1%)	--	
	Missing	--	2 (2%)	--	
In utero exposure to AZT, d4T, ddI, or ddC		--	75 (90%)	--	

All continuous variables expressed as median (interquartile range) and categorical variables as n (%). ART=antiretroviral therapy; ARVs=antiretrovirals; BMIZ=Body Mass Index z score; HAZ=Height-for-age z score; INSTI=Integrase Strand Transfer Inhibitor; NHANES=National Health and Nutrition Examination Survey; NRTI=Nucleoside Reverse Transcriptase Inhibitor; NNRTI=Non-nucleoside reverse transcriptase inhibitor; PI=Protease Inhibitor; SMARTT=Surveillance Monitoring of ART Toxicities; WAZ=Weight-for-age z score; wk=weeks; yr=years

FIGURE. DERIVATION OF ANALYTIC SUBGROUPS IN SMARTT AND NHANES



RESULTS

- **Overall characteristics of participants were similar between groups in all analytic subgoups, but SMARTT participants were more likely to report an annual household income <$20,000 in all samples (*p*<0.01 for all samples). (Table 1)**
- **Among SMARTT participants, >86% in all samples had *in utero* exposure to zidovudine, stavudine, didanosine, or zalcitabine.**
- **After adjusting for confounders, SMARTT youth had higher rates of systolic and diastolic HTN (PR=3.34, 95% Confidence Interval (CI): 2.48, 4.50; PR=2.04, 95%CI: 1.18, 3.52 respectively) but lower rates of insulin resistance (IR) (PR=0.69, 95%CI: 0.55, 0.88) and hypercholesterolemia which trended towards significance (PR=0.68, 95%CI: 0.44, 1.01). (Table 2)**

TABLE 2. MODELS OF MEAN DIFFERENCES AND PREVALENCE RATIO ESTIMATES COMPARING SMARTT VS. NHANES FOR EACH METABOLIC OUTCOME

Model	Mean difference (95% CI)	*p*-value	Prevalence Ratio (95% CI)	*p*-value
Systolic BP z-score	0.64 (0.52, 0.75)	<0.01	3.34 (2.48, 4.50)	<0.01
Diastolic BP z-score	0.72 (0.61, 0.83)	<0.01	2.04 (1.18, 3.52)	0.01
HDL	-0.41 (-1.66, 0.85)	0.52	1.30 (0.85, 1.88)	0.25
Total Cholesterol	-5.49 (-8.98, -1.99)	<0.01	0.68 (0.44, 1.01)	0.06
LDL	-1.60 (-8.90, 5.71)	0.67	0.98 (0.38, 2.54)	0.96
Triglycerides	-2.14 (-12.12, 7.85)	0.67	1.00 (0.40, 2.49)	1.00
HOMA-IR	-1.73 (-2.47, -0.99)	<0.01	0.69 (0.55, 0.88)	<0.01

**All models adjusted for age, body mass index z score, sex, and black race. BP=Blood Pressure; CI=Confidence Interval; HDL=High-Density Lipoprotein-C; HOMA-IR=Homeostatic Model Assessment-Insulin Resistance; LDL=Low-Density Lipoprotein-C*

CONCLUSIONS

- **Obese HEU youth appear to be at higher risk for HTN, but lower risk for hypercholesterolemia and IR, compared to a matched obese U.S. population.**
- **Further studies are warranted to understand the causes and long-term implications of these findings.**

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