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Risk Factors for Cardiovascular Disease in Human Immunodeficiency Virus-1 Infected Children

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Abstract

Objective—To determine risk factors for cardiovascular disease (CVD) in HIV-infected children compared with nationally representative controls from 2003–2004 NHANES data.

Study design—Prospective, longitudinal analysis of CVD risk factors in 42 HIV-infected children compared with NHANES controls with multivariable modeling of demographic, disease-specific, and treatment-related factors contributing to cardiac risk in the HIV cohort.

Results—The 42 HIV-infected children were initially an average of 10.1 years old, 68% CDC class B or C, and 76% were on HAART. Compared with age- and sex-adjusted NHANES controls, HIV-infected children had lower weights (−.46 SD vs +.54 SD; $P < .001$), heights (−.62 SD vs +.26 SD; $P < .001$), and body mass index (−.09 SD vs +.51 SD; $P < .001$). HIV-infected children had higher triglycerides (136 mg/dL vs 90 mg/dL; $P < 0.001$) and lower HDL-cholesterol levels (47 mg/dL vs 54 mg/dL; $P < 0.001$). Protease inhibitor (PI) therapy was independently associated with higher triglycerides ($P = 0.02$) and LDL-cholesterol ($P = 0.04$) and lower HDL-cholesterol ($P = 0.02$); NNRTI therapy was associated with lower visceral fat ($P = 0.01$) and higher HDL-cholesterol ($P = 0.005$).

Conclusions—HIV-infected children, compared with NHANES controls, have adverse cardiac risk profiles. Antiretroviral therapy has significant effects on these factors.

Keywords

Child; HIV - AIDS; Cardiovascular Risk Factors; Lipids; Abdominal fat

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Since the introduction of highly active antiretroviral therapy (HAART), HIV disease in developed nations has transitioned from an almost uniformly fatal illness to a chronic disease with therapies now targeted toward indefinite viral suppression (1). Although certain adverse metabolic outcomes were present before the advent of HAART, these abnormalities have increased both in prevalence and scope (2). These metabolic problems have been better described in adults (3), with more limited data in children (4–9).

There is evidence that adults with HIV infection are at an increased risk of developing premature atherosclerotic CVD associated with abnormal metabolic profiles (2,10). Factors cited as potential contributors to increased cardiovascular risk in adults include specific HAART therapy, sex, age, lifestyle habits (exercise, smoking), and prior history of CVD (10–12). Even less is known about cardiovascular risk in children with HIV. Compared with the pre-HAART era (13), studies in children have shown that PIs improve weight (14) but may be associated with increased serum levels of fasting lipids (5,15). However, specific drug effects and visceral adiposity (4,16), known cardiovascular risk factors in adults, have not been assessed well in children.

As children live longer with HIV and undergo more intensive and potentially cardiotoxic therapies, cardiac morbidity and mortality may become an increasing problem. In this prospective study, our goal was to identify the cardiac risk factors and anthropometric differences in HIV-infected children compared with a national cohort (NHANES 2003–2004) and to identify characteristics of HIV-infected children and their treatment course that lead to abnormal cardiac risk factor profiles.

METHODS

Cases, Controls, and Data Collection

Children with HIV were enrolled in a National Institute of Diabetes, Digestive and Kidney Disease-supported prospective, longitudinal study on growth and nutrition at the Children's Hospital AIDS Program in Boston, MA (n=25), and at the University of Rochester Pediatric HIV Program in Rochester NY (n=17). The 2003–2004 NHANES database, (US Department of Health and Human Services Centers for Disease Control (CDC) National Health and Nutrition Examination Survey, 2003–2004) was used to identify a control population of children. A total of 4437 NHANES children between the ages of 1 and 19 years were used to determine mean values of our outcomes of interest. These 4437 control children are representative of a national sample of 77 479 681 children. In addition, a smaller group of 16 demographically-matched HIV-negative siblings or friends were recruited at the same time and studied for similar outcomes. The Institutional Review Boards at both institutions approved all research protocols, and informed consent from the parent or guardian and assent from the patient (when appropriate) were obtained.

Study visits for the HIV-infected children occurred at an NIH General Clinical Research Center between November 1997 and October 2003 (both centers). Clinical data for all children (HIV-infected and controls [when available]) included age, sex, race, weight, height, body mass index (BMI), skinfold thicknesses, waist and hip circumferences and fasting serum lipid profiles (total cholesterol, triglycerides, HDL-cholesterol, and LDL-cholesterol). Clinical data collected at the time of the visit for the HIV-infected children included Center for Disease Control (CDC) pediatric HIV disease stage (17), Tanner stage, and type of antiretroviral therapy (ART).

Laboratory assays included absolute CD4 T lymphocyte cell counts and plasma HIV-1 RNA concentration by quantitative HIV-1 RNA PCR (Amplicor HIV-1 Monitor test, Roche Diagnostic Systems, Branchburg, NJ). A single-slice computerized tomography (CT) scan was

performed on a subset of the HIV-infected children during the study period. Sociodemographic, clinical, and laboratory data were collected by trained research dietitians.

Anthropometric Measures

For the HIV-infected children, height, weight, mid-arm circumference (MAC), skinfold thicknesses, and waist and hip circumference measurements were obtained by registered dietitians trained in anthropometry and who attended training sessions to standardize techniques in anthropometry. Body mass index was calculated as weight (kg)/height² (meters). Skinfold thicknesses were measured with Lange skin calipers (Lange, Cambridge, MD) and MAC was measured with a plastic, non-stretchable tape using standard techniques (17). The average of three measurements for each skinfold region was recorded. Triceps skinfold (TSF) and MAC were used to derive arm muscle circumference (AMC) (18). Age- and sex-adjusted percentiles for TSF and AMC were calculated (19). Weight, height, and BMI were expressed as Z-scores (20).

Waist and hip circumferences were measured using a plastic non-stretchable tape. Waist circumference was measured at the navel during minimal inspiration. Hip circumference was measured at the maximal extension of the buttocks according to standard methods (21). Available comparable measurements for the NHANES control children were collected as described previously (21).

Single-Slice Computerized Tomography

For the HIV-infected children only, a single-slice scan of the abdomen was obtained to determine central adiposity. Abdominal scans were taken with a GE CTi single slice CT scanner (GE Medical Systems, Milwaukee, Wisconsin) as described previously (22). The area of total fat, intra-abdominal fat, and subcutaneous fat was analyzed with the images digitized by optical density to separate bone, muscle, lean tissue, and fat compartments using a modified version of the image program (version 1.38, NIH, Bethesda, Maryland). Pixel units were converted to area measurements using an internal calibration standard. Digitized images were analyzed in a blinded fashion centrally at Tufts University, Boston, Massachusetts. The coefficient of variation of repeated analyses of a single scan was 1.5%.

Statistical Methods

Anthropometric measures and lipid profiles were compared longitudinally between the HIV-infected children and NHANES controls, as well as between HIV-infected children and sibling controls, using a repeated-measures linear regression to account for longitudinal measurements within the HIV-infected cohort (Genmod procedure, SAS). The models were adjusted for age and sex, and the results are presented as estimated anthropometric and lipid values for a typical child.

Within the full cohort of 42 HIV-infected children only, we assessed the effects of anthropometry, age, sex, race, viral load, and therapies on longitudinally measured cardiac risk factors. For these analyses, cardiac risk factors included the results of single slice CT scans (VAT, SAT) and serum lipids. As above, repeated measures linear regression models were used to allow for serial correlation in the longitudinal cardiac risk outcomes. Tanner stage also was considered but was found to be non-significant for all endpoints and is not presented. Initial repeated measures regression models considered each of the risk factors separately, although all models were adjusted for age and sex. The final multivariable models were constructed with age, sex, race, BMI, viral load, and antiretroviral therapies entered simultaneously. The final models did not include the overall classification of “HAART” therapy because of its link with PIs, nucleoside reverse transcriptase inhibitors (NRTI) and non-nucleoside reverse transcriptase inhibitors (NNRTI).

RESULTS

Baseline Demographic and Clinical Characteristics

In all, 42 HIV-infected children were enrolled in the study. HIV infection was acquired perinatally in all HIV-infected children. The mean initial age of the 42 HIV-infected children at entry into this study was 10.1 years (range, 2.7 to 18.9 years), with 64% female, and the mean initial age of the NHANES controls was 8.8 years (range, 1.7 to 19.0 years), with 50% female. The racial distribution of the HIV-infected children was 48% African American, 19% Hispanic, 26% non-Hispanic white, and 7% other, while the NHANES controls were 15% African-American, 19% Hispanic, and 61% non-Hispanic white. Most of the 42 HIV-infected children had a history of symptoms of HIV—CDC stage A, $n = 13$ (31%); CDC stage B, $n = 18$ (43%)—or were diagnosed with AIDS—CDC stage C, $n = 10$ (24%). One child had asymptomatic disease (CDC stage N). Of the HIV-infected children, 68% were Tanner stage 1, 14% were Tanner stage 2 or 3, and 18% were Tanner stage 4 or 5. The median CD4 T-lymphocyte count was 780 cells/mm³ (interquartile range [IQR]: 321, 1073 cell/mm³) and median percent CD4 was 27% (IQR: 18, 38 %). The initial median HIV viral load was 4,088 copies/mL (IQR: 400, 38,545 copies/mL). Use of PIs was common ($n=33$; 79%; mean length of time on PI = 28 months). Initially, 95% of infected children ($n=40$) were receiving NRTI therapy (mean length of time = 34 months) and 29% ($n=12$) were receiving NNRTI (mean length of time = 23 months). Seventy-six percent ($n=32$) were on HAART as of their first visit. The HIV-infected children had a median follow-up of 12 months and a median number of 2 study measurements.

Anthropometric Characteristics

Anthropometry values were adjusted for age and sex (Table I). HIV-infected children were about one-half of a standard deviation below normal in weight and height Z-scores. The HIV-infected children were significantly lighter (1 SD), shorter (0.88 SD) and with a lower BMI (0.6 SD), compared with NHANES children. However, subscapular skinfold and waist circumferences were similar between the two groups of children despite BMI being 0.6 SD less in the HIV group. When the HIV group was compared with the smaller contemporary HIV-negative controls, height (-0.23 [se 0.32]), weight (-0.13 [se 0.37]), and BMI (0.17 [se 0.26]) z-scores were similar. However, significant differences were found with controls having higher TSF percent (62% [se 8.4]; $p=0.03$) and biceps skinfold thickness (8.8 [se -.99]; $p=0.03$) and lower waist to hip ratios (0.80 [se 0.01]; $p<0.001$).

Frequency of Cardiac Risk Factors

None of the HIV-infected children had clinical signs or symptoms of cardiac dysfunction (dyspnea on exertion, chest pain, respiratory distress, edema, hepatosplenomegaly). Fasting triglyceride levels were significantly higher in the HIV-infected children (136 mg/dL vs. 90 mg/dL; $P < 0.001$) (Table II). Furthermore, HDL-cholesterol levels were lower in HIV-infected children (47 mg/dL vs. 54 mg/dL; $P < 0.001$). Total cholesterol levels tended to be higher in the HIV-infected children ($P=0.129$). LDL-cholesterol levels were borderline significantly higher in HIV-infected children ($P=0.085$). These differences represent a 89% higher level of triglycerides and a 13% lower level of HDL-cholesterol in the HIV-infected group. When the HIV group was compared with the smaller contemporary HIV-negative controls, there were similar findings of lower triglycerides (contemporary controls 55.5 [se 7.80] mg/dL; $p<.001$) and HDL (contemporary controls 61.5 mg/dL [se 5.5] mg/dL; $p=0.01$).

Subcutaneous (S) and visceral (V) adipose tissue (AT) were calculated from single-slice computed tomography (Table II) in a subset of 36 HIV-infected children [60 scans] and 9 contemporary control subjects [9 scans]. VAT and SAT, tended to be lower in the contemporary controls, but difference was not statistically significant (VAT 20.2 cm² [se=2.8] vs 15.6 [se

1.9]; SAT 92.3 [se=13.3] vs 86.5 cm² [se=12.3]; HIV vs contemporary controls, respectively). For the HIV-infected children only, we performed analyses that showed, after adjusting for age and sex, that visceral adipose tissue was significantly associated with waist:hip circumference ratio. We also found that BMI correlated poorly with our outcomes (data not shown).

Univariable Predictors of Cardiac Risk Factors in HIV-Infected Children

Univariable analyses of the predictors of cardiac risk factors (SAT, VAT, HDL-cholesterol, LDL-cholesterol, and triglycerides for HIV-infected children alone) were adjusted for age and sex (Table III). Candidate predictors included race, CD4 percentage, log HIV viral load, and type of ART. For subcutaneous adipose tissue, older age ($P = 0.004$) and female sex ($P = 0.03$) were associated with higher subcutaneous adipose tissue values. Univariable predictors of lipid levels showed that PI therapy was associated with increased levels of triglycerides, and LDL-cholesterol; NRTI therapy was associated with increased SAT and VAT; HAART therapy was associated with increased levels of triglycerides; and NNRTI therapy was associated with increased HDL-cholesterol levels.

Multivariable Predictors of Cardiac Risk Factors in HIV-Infected Children

The multivariable models for SAT, VAT, and lipids, our cardiac risk factors, were adjusted for age, sex, race, viral load, ART use (Table IV). General demographic factors were independently associated with some of these outcomes. Specifically, older children had higher subcutaneous adipose tissue ($P = 0.01$). Girls had a higher risk of having increased subcutaneous adipose tissue ($P = 0.01$). Hispanics (compared with African Americans) had lower HDL-cholesterol ($P = 0.001$), whereas non-Hispanic white children, compared with African American children, had higher visceral adipose tissue ($P = 0.001$). BMI was positively associated with increases in SAT ($P < 0.001$) and VAT ($P < 0.001$). Children with a higher viral load had lower HDL-cholesterol levels ($P = 0.02$) and lower LDL-cholesterol levels ($P = 0.005$).

The PIs were independently associated with elevations in lipid profiles, including LDL-cholesterol ($P = 0.04$) and triglycerides ($P = 0.02$), with lower HDL-cholesterol levels ($P = 0.02$). NNRTIs were independently associated with higher HDL-cholesterol levels ($P = 0.005$) and lower visceral adipose tissue ($P = 0.01$). NRTIs were independently associated with higher VAT ($P = 0.04$). Because stavudine (an NRTI) was given almost exclusively in conjunction with PIs, we were not able to include both of these predictors in the multivariate model in Table IV. However, when stavudine was substituted for PI into the multivariate model, stavudine was associated with a significant increase in triglycerides, but not in HDL nor LDL. Also of interest, stavudine was associated with a significant increase in the VAT:SAT ratio in univariate analysis, and approached significance ($p = .053$) in the multivariate model.

DISCUSSION

We compared HIV-infected children and NHANES controls on several factors associated with increased risk for premature CVD. Our data show that, compared with NHANES controls, HIV-infected children have lower weights, heights and BMIs, but have similar waist circumferences and subscapular skinfold thicknesses. These findings may suggest a disproportionate higher waist circumference and subscapular skinfold (suggestive of fat redistribution) in our HIV-infected children. However, compared with a smaller, contemporary comparison group, we found heights, weights and BMIs to be similar. Furthermore, our study showed additional risk for premature CVD with higher triglycerides and lower HDL-cholesterol levels in the HIV-infected children (compared with both control groups). PI therapies were associated with adverse lipid profiles, NRTI therapies with greater visceral fat, and NNRTI therapies showed beneficial effects with higher HDL-cholesterol levels and lower

visceral adipose tissue. Visceral adipose tissue was significantly associated with waist:hip circumference ratio and BMI correlated poorly with our outcomes. This result may have particular importance in situations where measurement of visceral adipose tissue is impractical, but measurement of waist:hip ratio is simple and may serve as an adequate surrogate.

Before HAART, the majority of HIV-infected children were malnourished and cachectic (13,23), severely stunted (24), and had gastrointestinal (25) and systemic conditions that would sustain these abnormal nutritional states. With effective antiretroviral therapies, their nutritional condition has improved (14) and has shifted toward increased metabolic problems (4–6,9). First noted by Carr (3), the associations of effective ART and metabolic problems documented in adults now are recognized increasingly in children with HIV. Our data confirm existing data and bring new information regarding clinical comparisons between HIV-infected children and national controls, as well as define cardiovascular risk effects of specific classes of ART.

Hyperlipidemia in HIV-infected children was reported before HAART (26). However, lipid abnormalities have become more pronounced since the advent of HAART (5,15). PIs, specifically, have been associated with elevations in cholesterol and triglycerides (27). In adults with HIV, where the likelihood of myocardial infarction is increased by age alone, studies have shown that the risk of CVD increases substantially for every year on ART (2,10,12). Hyperlipidemia at an early age in childhood is expected to lead to early CVD (28,29).

Studies of HIV-infected children among centers have shown that abnormal fat distribution defined as a shifting of body fat to the abdomen and dorsocervical fat pad and depletion of adipose tissue of the face, limbs and buttock (3)-- can occur in 17% to 33% (6,8). In some studies of adults, more than 50% of patients have clinically obvious lipodystrophy, depending on the definition (3). Fat redistribution can be defined clinically, through skinfold measurements, or rarely through dual x-ray absorptiometry scanning. However, these measures are rough estimates, and investigations of visceral and subcutaneous adiposity in HIV-infected children through more sensitive techniques (such as single-slice CT or MRI) have been limited (16). Although no standards for visceral and subcutaneous fat are available for children, we found that girls have a greater subcutaneous adipose tissue and non-Hispanic whites have greater amounts of visceral fat in our sample, findings that have been substantiated in other non-HIV studies (30–32). Furthermore, NNRTIs were found to be protective against, yet NRTIs associated with, higher visceral adipose tissue levels.

We found that use of different classes of medications (PI, NRTI, NNRTI) influences cardiovascular risk profiles in different ways. PIs appeared to have more adverse effects on lipid profiles. These findings were described early in adults with HIV (2), and some associations have been found in children (15,33). Such therapy may have direct influence on lipid levels by inhibiting an LDL-cholesterol receptor-related protein that blocks the uptake of lipoproteins and their subsequent metabolism (34) or increases apolipoprotein B metabolism (35). Other theories include stimulation of VLDL-cholesterol synthesis by PIs, adipogenesis, or lowering the expression of insulin receptors on adipocytes, thus increasing release of free fatty acids with the potential for inducing hepatic production of lipoproteins (34). NRTIs appear to increase VAT, which has been associated with increased CVD risk. Viral load appeared to uniformly increase cholesterol levels (total [data not shown], HDL, and LDL); effects that have been shown to be beneficial (HDL) and adverse (total, LDL) on CVD risk.

Lastly, we found that NNRTI therapy may have protective effects by decreasing visceral adipose tissue and increasing HDL-cholesterol. The protective effects of NNRTI have been noted in adults (36). In studies of PI-switching regimens, improvements in lipid levels tend to be more substantial with nevirapine than with efavirenz; this tendency was also observed when

nevirapine was used in initial treatment regimens. Further, in the first pediatric SWITCH study, McComsey noted that LDL- and total cholesterol as well as triglycerides decreased in a small number of children whose therapy was changed from a PI to NNRTIs (37).

We did not have sufficient sample size to evaluate the independent effects of combined ART. Rather we determined specific effects of each class of drug rather than their combined effects. We collected data to evaluate our study hypothesis that age, race, sex, Tanner stage, BMI, HIV disease status, HIV viral load, and the use of specific antiretroviral therapies would affect risk factors for premature symptomatic CVD. The number of significant associations ($P < 0.05$) given in Table IV is greater than would be expected by chance if there were no associations in the data. Because these associations are exploratory and the sample size is small, and since these associations were determined *a priori* in our study, we have not adjusted the Type I error to account for multiple comparisons, thus the P-values should be interpreted cautiously.

Children with HIV infection, compared with NHANES and contemporary controls, have adverse cardiac risk factors. We found that PIs and NRTIs contribute to these abnormal profiles, whereas NNRTIs have protective and beneficial effects on these risks in our study. Because readily accessible anthropometric measures such as BMI did not correlate well with metabolic outcomes, HIV-infected children should be proactively monitored for the emergence of these risk factors, regardless of BMI percentiles. Interventions that improve cardiac risk profiles including modifications of lifestyle, such as exercise (37) and diet, that are known to benefit other populations, should be considered.

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Table I

Anthropometry of HIV-Infected Children and NHANES (2003–2004), Adjusted for Age and Sex

Variable	HIV (se) N=42	NHANES (se) N=4437	P-value
Height Z-score	−0.62 (0.24)	0.26 (0.03)	<0.0001
Weight Z-score	−0.46 (0.18)	0.54 (0.03)	<0.0001
BMI Z-score	−0.09 (0.12)	0.51 (0.04)	<0.0001
TSF %	43 (3.6)	n/a	n/a
Biceps skinfold (mm)	6.4 (0.60)	n/a	n/a
Subscapular skinfold (mm)	10.4 (1.3)	10.89 (0.22)	0.709
Suprailiac skinfold (mm)	15.0 (1.7)	n/a	n/a
AMC %	50 (4.2)	n/a	n/a
Waist measurement (cm)	66.0 (1.7)	68.67 (.46)	0.130
Hip measurement (cm)	74.5 (1.8)	n/a	n/a
Waist:hip ratio	0.89 (0.014)	n/a	n/a

BMI = body mass index

TSF = triceps skinfold

AMC = arm muscle circumference

Table II

Age and Sex-Adjusted Comparisons of Cardiac Risk Factors between HIV-Infected Children and NHANES (2003–2004) Controls

Risk Factor	HIV-Infected N=42	NHANES N=4437	P-value
Triglycerides (mg/dL)	135.9 (13)	89.59 (2.66)	<0.001
Cholesterol (mg/dL)	172.3 (6.2)	162.8 (0.84)	0.12
HDL (mg/dL)	46.8 (2.0)	54.15 (0.46)	<0.001
LDL (mg/dL)	97.9 (4.9)	89.27 (1.01)	0.085
VAT (cm ²)*	20.2 (2.8)	n/a	n/a
SAT (cm ²)*	92.3 (13.3)	n/a	n/a

P values are from repeated measures linear regression models, adjusted for age and sex. Effect estimates are covariate-adjusted means (least-squares means) with standard errors.

* VAT and SAT measures were obtained from 36 HIV-infected children (60 measures)

VAT = visceral adipose tissue

SAT = subcutaneous adipose tissue

Table III
Age and Sex-Adjusted Univariate Repeated Measures Predictors of Cardiac Risk Factors in HIV-Infected Children*

Children/visits Predictor	SAT (cm ²) 36 / 60 Effect (se)	VAT (cm ²) 36 / 60 Effect (se)	Triglycerides (mg/dL) 41 / 79 Effect (se)	HDL (mg/dL) 37 / 67 Effect (se)	LDL (mg/dL) 37 / 67 Effect (se)
Age (mos)	.95 (.33)²	.12 (.08)	.33 (.38)	-.04 (.17)	-.18 (.11)
Female	54 (25)¹	3.6 (6.2)	-5.0 (28)	-4.4 (4.1)	12 (10)
White**	18 (35)	13 (8.4)	46 (44)	-3.2 (5.7)	-.52 (16)
Hispanic**	55 (50)	14 (8.0)	15 (24)	-12 (3.1)³	-2.5 (10)
Log VL (copies/mL)	-6.4 (4.0)	-.98 (.89)	3.3 (4.8)	-.92 (.68)	-5.1 (1.5)³
PI	16.3 (24)	5.4 (6.5)	71 (25)²	-4.0 (4.1)	22 (8.2)¹
Stavudine	12.8 (27)	8.6 (6.3)	67 (30)¹	-0.4 (3.6)	6.2 (9.3)
NNRTI	61 (30)¹	14 (5.6)¹	11 (60)	8.0 (13)	6.1 (9.8)
NNRTI	-18 (24)	-6.8 (4.5)	-14 (24)	8.3 (4.0)¹	11 (9)
HAART	-5.0 (28)	5.8 (6.9)	101 (24)³	-2.9 (4.1)	15 (10)

* Values in bold represent significant effects

** Compared to Blacks (reference)

¹ P<0.05

² P<0.005

³ P<0.001

VL=viral load

VAT=visceral adipose tissue

BMI=body mass index

NNRTI=non-nucleotide reverse transcriptase inhibitor

PI=protease inhibitor

SAT=subcutaneous adipose tissue

HAART=highly active antiretroviral therapy

Table IV
Multivariable Repeated Measures Models for Cardiac Risk Factors in HIV-Infected Children*

Predictor	SAT (cm ²) Effect (se)	VAT (cm ²) Effect (se)	Triglycerides (mg/dL) Effect (se)	HDL (mg/dL) Effect (se)	LDL (mg/dL) Effect (se)
Age (mos)	.74 (.27) ²	-.04 (.04)	.27 (.38)	-.04 (.05)	-.14 (.14)
Female	40 (16) ²	6.3 (4.0)	-15 (33)	.46 (3.2)	10 (10)
White**	31 (27)	13 (3.3) ⁴	27 (39)	-3.8 (4.4)	-13 (18)
Hispanic	11 (31)	-6 (5.0)	12 (31)	-10.2 (3.1) ⁴	-6.3 (12)
BMI Z score	52 (8.4) ⁴	10 (1.5) ⁴	-16.7 (13)	-1.09 (1.8)	1.3 (4.8)
Log(VL)	-1.5 (2.5)	.19 (.61)	2.9 (3.9)	-1.2 (.50) ¹	-4.9 (1.7) ³
PI	4 (23)	-3.5 (3.5)	70 (31) ¹	-8.9 (3.9) ¹	15 (7.5) ¹
NNRTI	-26 (17)	-7.5 (3.0) ²	-20 (28)	8.2 (2.9) ³	4.9 (10)
NRTI	49 (27)	11 (5.6) ¹	-23 (41)	16 (13)	8.1 (13)

* values in bold represent significant effects.

** Compared to Black (reference)

¹ P≤0.05

² P≤0.01

³ P≤0.005

⁴ P≤0.001

Log(VL) = log viral load

VAT = visceral adipose tissue

SAT = subcutaneous adipose tissue

BMI = body mass index

PI = protease inhibitor

NNRTI = nucleoside reverse transcriptase inhibitor

NNRTI = non- nucleoside reverse transcriptase inhibitor