

Leg Fat Is Decreased but Arm Fat is Increased in HIV-Infected Children and Adolescents Receiving Antiretroviral Medications

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BACKGROUND

- Lipodystrophy is reported in approximately 25-30% of HIV-infected children and adolescents.
- Prior studies have used a variety of more or less objective methods and criteria to ascertain incidence and prevalence of abnormalities in regional fat distribution including: clinical observations and physical exam, skin fold and circumference based case definitions normalized against age and sex standards, laboratory methods including dual x-ray energy absorptiometry (DXA) and MRI.
- An important challenge in studies of regional fat changes in growing children and adolescents with HIV is to distinguish normal changes related to growth and sexual maturation from those related to disease or drug exposure. Few studies have adequately addressed this.

OBJECTIVE

The objective of this study was to characterize and compare changes over 2 years in total and regional fat measured by DXA in HIV-infected and healthy children and adolescents.

METHODS

Subjects:

- HIV-infected subjects were recruited from among perinatally-infected children and adolescents enrolled in 4 hospital-based pediatric HIV treatment programs in New York City.
- Healthy volunteers were enrolled in the Bone Mineral Density in Childhood Study by advertisement in local newspapers, school newsletters, flyers in nearby hospital waiting rooms and words of mouth.

Measurements:

- Total, leg, arm, and trunk fat masses in grams and fat distribution as the percent of total body fat (% of total) in each region were measured by dual energy x-ray absorptiometry (DXA) scans (Hologic Delphi) at enrollment and 2 annual visits.
- Pubertal status was determined by the method of Tanner.
- HIV disease classification was determined using CDC criteria.

Statistics:

- Baseline characteristics were compared using chi-square and non-parametric tests.
- Repeated measures models were used to compare arm, leg, and trunk fat (% of total body fat) between HIV+ and healthy children over three time periods.
- Classification of changes in regional fat between visits was determined based on whether the observed change exceeded CV of DXA.
- Multivariate repeated measures models were developed for longitudinal DXA measures; model selection done by considering all possible subsets of variables as well as interactions between significant predictors.

1. Baseline characteristics of subjects

- Sixty-four HIV+ and 147 HIV- subjects ages 6-16 yr were enrolled.
- HIV+ and HIV- subjects were similar at baseline with respect to pubertal stage, sex, height-for-age, and weight-for-age.
- However, the HIV+ group was younger, and had a greater proportion of African Americans.
- All HIV+ subjects were infected perinatally and were receiving 2 or more ARVs.
- The mean (SD) baseline CD4 number was 786 (365) and among those with detectable viral load (38%), the mean (SD) baseline viral load was 3.35 (0.72) log copies/mL.

	Healthy n=157	HIV-infected n=64	p-value
	No. or Mean (% or STD)	No. or Mean (% or STD)	
Age	11.6 (2.8)	10.3 (2.7)	0.002
Male	73 (49.7)	31 (48.4)	0.870
Female	74 (50.3)	33 (51.6)	
Black	71 (48.3)	44 (68.8)	0.006
Hispanic	76 (51.7)	20 (31.3)	
Pubertal Stage: Girls			
Tanner stage <3	31 (41.9)	13 (39.4)	0.806
Tanner stage ≥3	43 (58.1)	20 (60.6)	
Pubertal Stage: Boys			
Tanner stage <3	45 (62.5)	19 (61.3)	0.908
Tanner stage ≥3	27 (37.5)	12 (38.7)	
Height age %-tile	55.7 (25.9)	50.4(28.4)	0.208
Height Z-score	0.2 (0.8)	-0.01 (1)	0.159
Weight age %-tile	60.8 (24.3)	62.0 (29.1)	0.770
Weight Z score	0.3 (0.8)	0.4 (1.1)	0.467
BMI %-tile	60.6 (23.9)	65.7 (28.1)	0.205
BMI Z-scores	0.3 (0.8)	0.5 (1.2)	0.130

2. Baseline body composition by DXA of Healthy and HIV-infected subjects

- HIV+ and HIV- did not differ in total fat mass or trunk fat as % of total
- HIV+ group had significantly lower leg and greater arm fat as % of total at baseline, 1 and 2 yr compared to the HIV-group. (data for years 1 and 2 not shown)

	Healthy Subjects (n=157)		HIV Infected (n=64)		p-value
	Mean or Median	SD or IQR	Mean or Median	SD or IQR	
Height, cm	146.04	16.99	141.70	15.54	0.077
Weight, kg	41.75	15.25	39.53	11.92	0.545
Total Fat, kg*	8.86	6.62	8.43	4.33	0.624
Total Fat, % of Weight*	22	10	22	09	0.944
Arm Fat, kg*	0.92	0.92	0.99	0.78	0.372
Leg Fat, kg*	4.26	3.29	3.73	2.10	0.049
Trunk Fat, kg*	2.58	2.47	2.52	1.83	0.939
Arm/Total Fat*	0.11	0.02	0.13	0.03	<0.001
Leg/Total Fat*	0.47	0.06	0.44	0.09	0.002
Trunk/Total Fat*	0.31	0.06	0.32	0.10	0.368

*Median and Interquartile Range (IQR) used.

RESULTS

3. Pattern of change in regional fat between baseline and year 2

- Differences in the patterns of change in leg, arm, and trunk fat (as % of total) were seen in the HIV infected and healthy subjects between baseline and years 1 and 2 follow up (baseline to year 1 not shown).
- Decrease in leg fat % and increase in arm fat % were more frequent among HIV-infected subjects whereas increase in leg fat % and decrease in arm fat % was more common among healthy subjects.
- There were no differences in the pattern of changes in trunk and total fat as % of body weight.

Region/direction of change	HIV Infected (n=49)	Healthy (n=117)	p-value
Leg fat (%)	n (%)	n (%)	
Decrease	21 (43)	28 (24)	0.037
No change	7 (14)	30 (26)	
Increase	21 (43)	59 (50)	
Arm fat (%)			
Decrease	13 (27)	59 (50)	<0.001
No change	10 (20)	37 (32)	
Increase	26 (53)	21 (18)	
Trunk fat (%)			
Decrease	12 (24)	21 (18)	0.436
No change	15 (31)	47 (40)	
Increase	22 (45)	49 (42)	
Total fat (%)			
Decrease	16 (33)	33 (28)	0.660
No change	8 (16)	26 (22)	
Increase	25 (51)	58 (50)	

4. Multivariate models for predicting % fat in each compartment.

Differences in arm and leg fat as % of total fat remained significant when age, sex, race, height, and pubertal stage were accounted for by mixed effect modeling. The table below shows the models developed for arm, leg, and trunk fat, each as a percent of total fat. Two models (arm and leg fat) contain interaction terms, indicating that age and height (respectively) operate together with HIV in the respective compartment.

Predictors	Model for Arm Fat/Total Fat			Model for Leg Fat/Total Fat			Model for Trunk Fat/Total Fat		
	Coefficient	SE	p-value	Coefficient	SE	p-value	Coefficient	SE	p-value
HIV infection	-0.009	0.010	0.4116	0.150	0.049	0.0022	0.031	0.007	<0.001
Female sex	0.008	0.003	0.0036	-	-	-	0.025	0.006	0.0001
Pubertal Stage > 3	-0.006	0.002	0.0139	-	-	-	-	-	-
Non-Black race	-	-	-	-0.016	0.0068	0.008	0.026	0.006	<0.001
Age*HIV infection	0.003	0.001	0.0007	-	-	-	-	-	<0.001
Height	-	-	-	0.073	0.017	<0.001	-	-	-
HIV infection*Height	-	-	-	-0.136	0.033	<0.001	-	-	-

* denotes the interaction effect of both variables in combination. For significant interactions, main effect terms are included even when not significant; e.g., HIV infection and age are included for arm/total fat since the age-HIV interaction is significant.

- indicates that the effect was not significant in the given model; e.g., sex was not a significant predictor of leg fat/total fat.

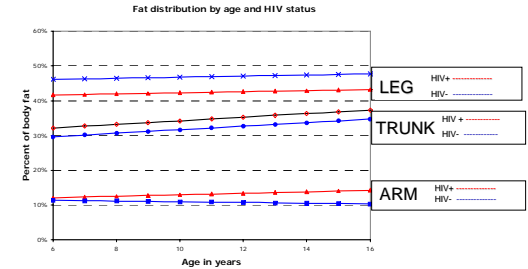
5. The interrelationships between predictors and regional fat are as follows:

Percent arm fat: HIV+ group has increased percent arm fat as compared with uninfected subjects; this effect increases by about 0.3% for each year of age, from a 0.9% increase at age 6 to 3.9% at age 16.

Percent leg fat: Height is associated with greater leg fat, however this relationship is modulated by HIV status. Subjects who are HIV+ have **decreased** percent leg fat as compared with uninfected subjects and this reduction becomes more pronounced as height increases (by -0.136% for each meter of height, e.g. from a 1.3% decrease at 1.2m HIV+ subjects have 1.3% less leg fat than healthy subject this difference increase to 5.4% at 1.5m).

Percent trunk fat: Trunk fat is consistently about 3.1% higher for subjects who are HIV+ (independent of age or height).

This figure illustrates the increased differences with age in arm fat as % of total fat.



CONCLUSIONS

- Serial objective measurements performed by DXA over 2 years confirm that despite having similar body fat content (e.g. total body fat %), perinatally HIV-infected youth have differences in the pattern of regional fat distribution compared to healthy subjects.
- Decreases in percent leg fat and increases in percent arm fat are more commonly seen in HIV-infected compared to healthy children and adolescents. These findings persist when other factors such as race/ethnicity, stage of sexual maturation and growth are accounted for.
- The magnitude of the differences between the HIV+ and healthy children and adolescents in arm and leg fat increases with greater age and height.
- It is important that future studies include objective measurements of regional fat and for changes in regional fat distribution that accompany growth and sexual maturation be accounted for.
- Long term studies of alterations in regional fat distribution and the significance these findings to glucose metabolism are warranted.

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