

## METABOLIC ABNORMALITIES IN YOUNG BEHAVIORALLY HIV-INFECTED WOMEN: Preliminary Results of Adolescent Medicine Trials Network for HIV/AIDS Interventions (ATN) – ATN021

Kathleen Mulligan<sup>1</sup>, Dina Monte<sup>2</sup>, D. Robert Harris<sup>2</sup>, Sonia Stoszek<sup>2</sup>, Patricia Emmanuel<sup>3</sup>, Dana S. Hardin<sup>4</sup>, Bill G. Kapogiannis<sup>5</sup>, Carol Worrell<sup>5</sup>, Craig M. Wilson<sup>6</sup>, Grace M. Aldrovand<sup>7</sup> for the ATN021 Protocol Team

<sup>1</sup>University of California, San Francisco, CA; <sup>2</sup>Westat, Rockville, MD; <sup>3</sup>University of South Florida, Tampa, FL; <sup>4</sup>The Ohio State University, Columbus, OH; <sup>5</sup>National Institute of Child Health and Human Development, NIH, Bethesda, MD; <sup>6</sup>University of Alabama at Birmingham, Birmingham, AL; <sup>7</sup>Childrens Hospital of Los Angeles, Los Angeles, CA

Kathleen Mulligan, PhD  
University of California, San Francisco  
San Francisco General Hospital B30, R3501K  
1001 Potrero Avenue  
San Francisco, CA 94110  
kathleen.mulligan@ucsf.edu

### ABSTRACT

**Aim:** Rates of HIV infection as well as obesity and metabolic disorders are increasing in young women of color. We evaluated the nature and scope of metabolic abnormalities and their association with antiretroviral therapy (ART) and lifestyle factors among young women (age 14-24yrs) infected with HIV through risk behaviors.

**Methods:** HIV+ women (>17y and seronegative controls (hIVneg, hIV-) were recruited at 15 ATN sites. HIV+ women were categorized as ART-naive (N=85), NNRTI (N=34), PI (N=36), Non-NNRTI/PI (N=16). Measurements included fasting lipid, insulin, and glucose, oral glucose tolerance, high sensitivity c-reactive protein (hsCRP), fat distribution by dual energy x-ray absorptiometry, and ART and medical histories by interview and questionnaire. Results were compared across groups and within HIV+ groups by ANOVA. Means and SEs are race-adjusted.

**Results:** The median age of HIV+ women was 20 yrs; 77% were African-American, 30% smoked cigarettes, and only 2% reported exercising regularly. More than half of ART-naive women were overweight or obese (BMI >25 kg/m<sup>2</sup>). The PI group had a longer duration of HIV infection (median 4 yrs), lower nadir CD4 count, and higher peak VL. Lopinavir and raltegravir were the most commonly used PI; 20% were on abacavir. Triglycerides in all HIV+ groups were higher than hIVneg. Total cholesterol was higher in groups on NNRTI or PI than ART-naive. Despite a relatively short duration of HIV (4 yrs), ART-naive had higher triglycerides and lower HDL-C than HIVneg. hsCRP levels tended to be higher in all ART groups. Fasting and 2-hour glucose and insulin levels did not differ significantly among groups, nor did total or regional fat distribution.

**Conclusions:** Dyslipidemia was relatively prominent in the group of young HIV+ women. Coupled with high rates of obesity, lifestyle factors (smoking, inactivity) and elevated hsCRP, these factors may accelerate lifetime risk of cardiovascular disease. These results underscore the need for a multifaceted approach to addressing cardiovascular risk in this population.

### BACKGROUND

- The HIV epidemic among U.S. adolescents persists with estimated 20,000 new infections annually (*Hall JAMA 2008*)
- Behaviorally acquired infections occur disproportionately among ethnic and racial minorities
- In the younger age groups infections in females outnumber males (*Wilson J Adol Health 2001*)
- The prevalence of obesity is also increasing among U.S. adolescents
- Obesity, HIV infection, and its therapies increase risk of dyslipidemia, disorders of glucose metabolism, and inflammation.
- This cross-sectional study was designed to determine the nature and prevalence of these abnormalities among behaviorally HIV-infected and uninfected adolescent females

### PARTICIPANTS

- Adolescent women ages 12-24
- HIV+ women infected through high-risk behavior
- Seronegative controls in same age range
- Tanner 4 or 5
- Non-pregnant, non-lactating

#### Primary exclusion criteria:

- Pregnancy in past year
- Type 1 diabetes
- Anorexia/bulimia

### MEASUREMENTS

- Fasting lipids
- 2-h oral glucose tolerance test
- High sensitivity C-reactive protein (hsCRP)
- Anthropometry
- Whole-body DXA with central analysis
- Medical and ART history by interview and chart review
- Lifestyle by questionnaire

### STUDY GROUPS

#### HIV-positive

ART-naive	N=85	No antiretroviral therapy ever
NNRTI	N=34	NNRTI but no PI ≥3 mos; <6 mos PI & none in past year
PI	N=36	PI but no NNRTI ≥3 mos; <6 mos NNRTI & none in past year
NoPI/NonNNRTI	N=18	no PI or NNRTI ≥3 mos; <6 mos NNRTI or PI & none in past year

#### HIV-negative

N=61 recruited at same clinical sites as HIV+; from similar age and racial distribution

### DEMOGRAPHIC AND LIFESTYLE FACTORS

High prevalence of CVD risk factors in both HIV-positive and negative participants

	HIV-negative	HIV-positive	P-value <sup>1</sup>
N	61	173	
Median age (yr [range])	20 [15-24]	20 [14-24]	0.15
Race (%)			0.005
Black/AA	56	77	
White	18	7	
Other/Mixed	26	16	
Ever pregnant (%)	36	51	0.04
Ever/current drug use (%) <sup>2</sup>	36	59	0.002
Drink alcohol (%)	97	61	0.41
Smoke cigarettes (%)	34	35	0.97
Exercise regularly (%)	52	32	0.005
Family Hx type 2 diabetes	39	40	0.59
Family Hx heart disease (%)	29	33	0.63

<sup>1</sup>With the exception of age. P-values by chi-square; for age, T-test. <sup>2</sup>Primarily cardiovascular.

### HIV DISEASE-RELATED DATA

More advanced disease in groups on ART

	ART-naive	PI	noPI/NonNNRTI	P-value <sup>1</sup>
N	85	34	36	18
Yrs HIV+ <sup>2</sup>	0.9	2.9	3.9	2.7
Current CD4	499	467	469	488
Nadir CD4	456	244	250	277
Current HIV RNA	6,000	200	200	200
Peak HIV RNA	13,400	42,960	72,750	35,430
CDC stage (%)				0.0003

Data are medians unless noted otherwise

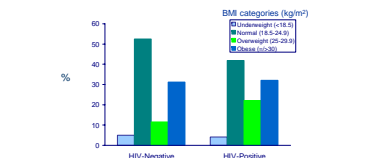
#### ART Regimens:

NNRTI: Efavirenz 47%, Nevirapine 50%, 3TC 94%, ZDV 73%  
PI: Nelfinavir 58%, Lopinavir 25%, other Ritonavir 17%, Atazanavir 19%, 3TC 52%, ZDV 72%

noPI/NonNNRTI: Abacavir 94%, 3TC 94%, ZDV 100%

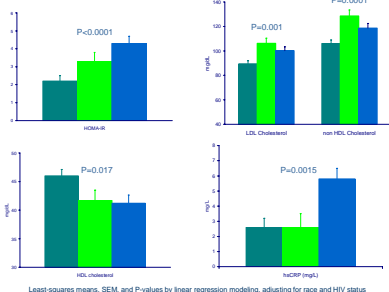
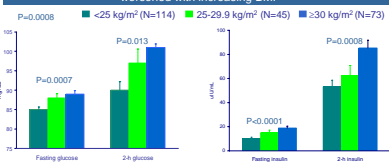
### BMI DISTRIBUTIONS

>40% of both HIV-positive and HIV-negative subjects were overweight or obese (BMI >25 kg/m<sup>2</sup>)



### METABOLIC DATA BY BMI GROUP

Indices of glucose metabolism, cholesterol, and inflammation worsened with increasing BMI



Least-squares means, SEM, and P-values by linear regression modeling, adjusting for race and HIV status

### METABOLIC DATA BY HIV/ART GROUP

- Lipids differed between HIV-positive and negative and within ART groups
- Despite relatively short duration of infection, HIV-infected, ART-naive participants had lower HDL-C and higher triglyceride levels, compared with HIV-negative
- No differences in glucose or insulin by HIV status or ART group
- hsCRP was higher in groups on ART: >40% on ART had hsCRP above the ULN

	HIV-negative	ART-naive	NNRTI	PI	NoNNRTI/NoPI	P-values Overall	HIV+ only
Lipids (mg/dL)							
Triglycerides	65±7	84±6*	129±9§	107±9*	96±12*	<.0001	.004
Total cholesterol	154±4	152±3	167±5§	173±5*	149±7	.003	.003
HDL-C	48±2	40±1*	43±2*	46±2	39±3*	.001	.12
LDL-C	93±4	95±3	95±5	106±5*	91±7	.19	.17
Non HDL-C	106±4	112±3	124±5*	127±5*	110±8	.009	.06

	HIV-negative	ART-naive	NNRTI	PI	NoNNRTI/NoPI	P-values Overall	HIV+ only
Indices of glucose metabolism							
Glucose (mg/dL)							
Fasting	88±1	85±1	88±1	86±1	87±2	.17	.34
2-hour	92±3	93±3	94±4	98±4	105±6	.28	.30
Insulin (µU/mL)							
Fasting	15±2	12±1	15±2	12±2	17±3	.18	.10
2-hour	66±7	63±6	65±10	64±10	73±13	.97	.93
HOMA-IR	3.4±0.4	2.5±0.4	3.5±0.6	2.6±0.5	4.3±0.8	.15	.09
hsCRP (mg/L)	2.2±0.8	2.9±0.7*	5.6±1.1*	3.8±1.1	7.9±1.5*	.005	.03

Race-adjusted means ± SEM. P-values from linear regression modeling. Overall P-values refer to comparisons among all 5 groups. P-values for HIV+ only refer to comparisons among the 4 HIV-positive groups only. HOMA-IR: homeostasis model of insulin resistance; hsCRP: high-sensitivity C-reactive protein. \*P<0.05 vs HIV-negative; §P<0.05 vs ART-naive

### MORPHOLOGIC DATA BY HIV/ART GROUP

Few differences between HIV-positive and negative groups or among HIV-positive groups

	HIV-negative	ART-naive	NNRTI	PI	NoNNRTI/NoPI	P-values Overall	HIV+ only
Anthropometric measurements							
BMI (kg/m <sup>2</sup> )	26.5±0.8	27.5±0.8	29.4±1.3	28.0±1.3	26.2±1.8	4.3	.47
Waist circumf (cm)	81±2	86±2	92±3	91±3	86±4	13	.22
Hip circumf (cm)	103±2	103±2	108±3	105±3	98±4	30	.19
Waist/hip ratio	.81±0.2	.83±0.1	.85±0.2	.86±0.2	.93±0.3*	.012	.06

	HIV-negative	ART-naive	NNRTI	PI	NoNNRTI/NoPI	P-values Overall	HIV+ only
DXA measurements							
Total LBM (kg/m <sup>2</sup> )	25.3±0.5	25.6±0.4	27.3±0.7	26.1±0.7	25.8±1.0	23	.25
Total fat (%)	35.5±1.3	35.0±1.1	36.2±1.8	37.0±1.8	33.1±2.6	.77	.58
Trunk fat (kg/m <sup>2</sup> )	7.3±0.6	7.4±0.5	8.0±0.8	8.2±0.8	6.9±1.1	.79	.66
Arm fat (kg/m <sup>2</sup> )	1.6±0.1	1.6±0.1	1.7±0.2	1.7±0.2	1.5±0.3	.91	.84
Leg fat (kg/m <sup>2</sup> )	6.7±0.5	6.7±0.4	7.0±0.7	7.1±0.6	5.4±0.9	.61	.42

Race-adjusted means ± SEM. P-values from linear regression modeling. Overall P-values refer to comparisons among all 5 groups. P-values for HIV+ only refer to comparisons among the 4 HIV-positive groups only. DXA: dual-energy X-ray absorptiometry. \*P<0.05 vs HIV-negative

### SUMMARY

- Obesity, dyslipidemia, and inflammation were prominent in this group of behaviorally infected adolescent women with a relatively short duration of infection.
- Dyslipidemia was associated with HIV infection, ART, and increasing BMI.
- Alterations in glucose metabolism were associated primarily with increasing BMI but not HIV infection or ART.
- Elevations in hsCRP levels were associated with both ART and increasing BMI.
- BMI was not lower than seronegative controls, and there was little evidence of altered fat distribution.
- Overall the major impact of body habitus on metabolic outcomes is that of conventional obesity, rather than altered fat distribution.
- There was a high prevalence of classic risk factors for cardiovascular disease (family history, smoking, inactivity)
- Taken together, these findings underscore the need for a multifaceted approach to reducing cardiovascular risk in this population.

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