Metabolic Syndrome Exacerbates Central Arterial Stiffness in HIV-1 Infected Patients Receiving Antiretroviral Treatment But Not in HIV-1 Treatment-Naïve Patients in sub-Saharan Africa

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ABSTRACT

Metabolic syndrome (MetS), a clustering of cardiovascular risk factors, is becoming increasingly prevalent with HIV-1 in resource-limited settings, and higher rates are observed in HIV-1-infected patients who are undergoing antiretroviral treatment (ART). Increased blood vessel stiffness may contribute to heart disease in HIV-infected patients taking ART. Therefore, the aim of this study was to determine whether blood vessel stiffness is increased in HIV-1-infected patients treated with ART, and if so, whether the presence of MetS exaggerates arterial stiffness in this population. We recruited 42 patients from the Kilimanjaro Christian Medical Center (KCMC) in Moshi, Tanzania: 14 HIV-1-infected not on treatment, 28 HIV-1-infected patients on ART, and 11 healthy controls. Resting blood vessel stiffness was assessed while patients were lying down using standard techniques. Blood vessel stiffness was much higher in the HIV-1-infected patients treated with ART compared with HIV-1 patients not on treatment and control subjects. Interestingly, MetS exacerbated vessel stiffness in HIV-1 ART patients. The presence of the MetS worsens arterial stiffness in HIV-1 patients on ART, a finding that is not observed in HIV-1 patients with MetS who are not on antiretroviral medication. The combined influence of ART with MetS may accelerate the development of cardiovascular disease in HIV-1 patients in sub-Saharan Africa.

BACKGROUND

- HIV-1 infection is associated with increased cardiovascular disease risk (CVD) compared with the general population.
- Although the introduction of antiretroviral treatment has greatly improved quality of life for HIV-1 infected individuals, there is concern that it may confer added CVD risk.
- HIV-1 patients receiving these medications exhibit a greater risk of heart attack and stroke compared with HIV-1 untreated patients; this may be due to increased blood vessel stiffness.
- The adverse effects of antiretroviral medications on CVD appear to be mediated in part, by the metabolic syndrome (MetS), a clustering of metabolic disturbances including high levels of cholesterol, triglycerides, blood sugar; and insulin resistance and abdominal obesity.
- Higher rates of MetS have been observed in different ethnic groups across the world, and rates of this disorder are accelerating in medically underserved societies, especially in HIV-1 patients in sub-Saharan Africa.
- The combination of MetS in HIV-1 patients who are taking antiretroviral medications may increase arterial stiffness and thereby heighten their risk of CVD.
- However, to date, there are no studies investigating whether the presence of MetS contributes to arterial stiffness in HIV-1 infected patients who are taking antiretroviral medications in sub-Saharan Africa.

EXPERIMENTAL AIM

Therefore, the aim of this study was to determine whether blood vessel stiffness is increased in HIV-1-infected patients treated with antiretroviral medications, and if so, whether the presence of MetS exaggerates arterial stiffness in this population.

METHODS

Subjects

- Forty-two adults between the ages of 40-60 years.
  - 11 Control (documented HIV-1 negative)
  - 14 HIV-1 Treatment-naïve (no history of antiretroviral medications
  - 28 HIV-1 patients assigned antiretrovirals
- Participants were recruited from the Kilimanjaro Christian Medical Center (KCMC) in Moshi, Tanzania.
- All subjects provided written informed consent according to the guidelines of the University of Wisconsin – Eau Claire and the Kilimanjaro Medical center.

Inclusion Criteria

- normotensive
- sedentary
- non-diabetic
- normolipidemic
- free of overt cardiovascular disease and diabetes

HIV-1 Infected Adults

- Seropositive for the HIV-1 virus for a minimum of one year.
- CD4 T cell counts required for treatment naïve: >500 mm^3
- CD4 T cell counts to initiate antiretroviral medications: <350 cells/mm^3 based on World Health Organization guidelines.

Screening and Testing Procedures

- Medical history with physical examination
- Fasting blood lipids, cholesterol and glucose
- Body composition assessment (height, weight, percent body fat, waist and hip circumferences)
- MetS was established according to the International Diabetes Federation (IDF).

*Abdominal obesity must be present, in addition to two other risk factors for the IDF criteria.

Components of MetS	International Diabetes Federation Criteria
Abdominal Obesity	*Waist circumference ≥ 90 cm in men or ≥ 80 cm in women
Fasting Triglycerides	≥ 150 mg/dL
HDL-cholesterol	< 40mg/dL in men or < 50 mg/dL in women
Blood Pressure (BP)	Systolic BP ≥ 130 mmHg or diastolic BP ≥ 85 mmHg
Fasting Blood Glucose	≥ 100 mg/dL

Aortic Pulse Wave Velocity Protocol

- Resting supine measurement arterial stiffness was assessed by aortic pulse wave velocity (PWV) using an ultrasound technique and Doppler tonometry.
- PWV measurements were completed in the morning hours after an overnight fast for all subjects.

STATISTICAL ANALYSIS

Group differences in demographic, hemodynamic, anthropometric, metabolic, and pulse wave velocity data were determined by analyses of variance and Paired T test where appropriate. Data are presented as mean±SD. Statistical significance was set at $P<0.05$. Statistical analyses were performed using SPSS software version 18.0.

RESULTS

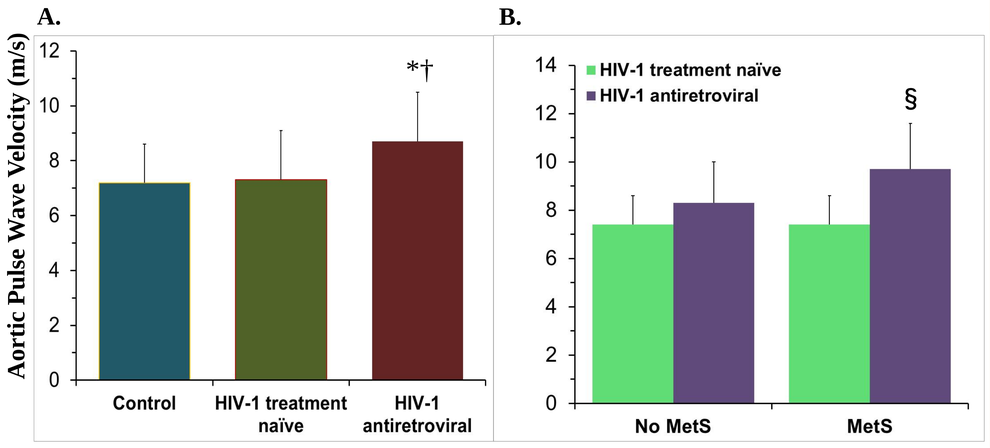
I. Subject characteristics for the entire study population

Variable	Control (n=12)	HIV-1 treatment naive (n=14)	HIV-1 antiretroviral treatment (n=28)
Age (years)	47±6	46±3	46±6
Height (cm)	168.9±11.6	163.9±6.3	162.2±7.6
Weight (kg)	76.8±5.3	74.5±2.9	73.7±3.5
BMI (kg/m^2)	21.9±3.5	25.2±4.9	25.2±5.2
Waist circumference (cm)	80.9±9.5	88.4±12.3	87.3±11.6
Systolic BP (mmHg)	118±9	130±11	124±12
Diastolic BP (mmHg)	72±8	77±6	76±8
Body fat (%)	27.9±9.1	34.7±8.4*	35.4±7.7*
MetS (%)	0	50	29
LDL-cholesterol (mmol/l)	2.2±0.5	2.1±0.8	2.5±0.9
HDL-cholesterol (mmol/l)	1.1±0.3	0.9±0.4	1.3±0.4
Triglycerides (mmol/l)	0.7±0.2	1.0±0.5	1.3±0.9
Glucose (mmol/l)	4.7±0.8	4.3±0.9	4.7±0.8
CD4 (mm^3)	615±114	688±164	446±247*†

* P<0.05 versus control; †P<0.05 versus treatment naive

III. Arterial stiffness was significantly higher in the HIV-1 antiretroviral subjects compared with control and HIV-1 treatment naïve subjects (A). In contrast to HIV-1 treatment naïve subjects, the presence of MetS worsened arterial stiffness in HIV-1 patients who were taking antiretroviral medications (B).

***P < 0.05 versus control; †P<0.05 versus treatment naïve; § P<0.05 versus treatment naïve MetS.**



SUMMARY AND CONCLUSIONS

- The presence of the MetS worsens arterial stiffness in HIV-1 patients on antiretroviral medications, a finding that is not observed in HIV-1 patients with MetS are treatment naive.
- The combined influence of antiretroviral medications with MetS may accelerate the development of cardiovascular disease in HIV-1 patients in sub-Saharan Africa.

ACKNOWLEDGMENTS

We would like to thank all of the participants for volunteering in our study and Drs. Gary Van Guilder and Titus Msoka for their assistance in our research efforts. This study was funded by a Student-Faculty International Fellows Program award for Research, Service, and Creative Activity in collaboration with the Office of Research and Sponsored Programs and the Center for International Education at UWEC.