HIV & Obesity

Gail Shor-Posner, PhD
Director, Division of Disease Prevention
Department of Epidemiology & Public Health
University of Miami Miller School of Medicine
What is Malnutrition?

Under-nutrition

Over-nutrition
Malnutrition
Wasting
HIV & Disease Progression

The early 80s

MALNUTRITION and WEIGHT LOSS → Suppressed immune system → HIV-DISEASE PROGRESSION and OPPORTUNISTIC INFECTIONS → MORTALITY
Benefits of Obesity in HIV Patients

<table>
<thead>
<tr>
<th>Variable</th>
<th>RR</th>
<th>95% CI</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI (time-dependent)</td>
<td>0.79</td>
<td>0.65–0.96</td>
<td>.02</td>
</tr>
<tr>
<td>Se&lt;sup&gt;a&lt;/sup&gt;</td>
<td>15.32</td>
<td>3.67–63.96</td>
<td>.0002</td>
</tr>
<tr>
<td>CD4 count &lt; 200 cells/mm&lt;sup&gt;3&lt;/sup&gt;&lt;sup&gt;a&lt;/sup&gt;</td>
<td>15.69</td>
<td>4.11–59.95</td>
<td>.0001</td>
</tr>
<tr>
<td>BMI (baseline)</td>
<td>0.75</td>
<td>0.60–0.95</td>
<td>.02</td>
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<tr>
<td>Se&lt;sup&gt;a&lt;/sup&gt;</td>
<td>12.93</td>
<td>3.13–53.38</td>
<td>.0004</td>
</tr>
<tr>
<td>CD4 count &lt; 200 cells/mm&lt;sup&gt;3&lt;/sup&gt;&lt;sup&gt;a&lt;/sup&gt;</td>
<td>17.48</td>
<td>4.43–69.04</td>
<td>.0001</td>
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</tbody>
</table>

<sup>a</sup> Time-dependent variables.

HIV Obesity & Disease Progression

Obesity among patients with HIV: The latest epidemic

Studies show that 6 out of 10 HIV+ people are overweight/obese

“More than 70% of the patients were on HAART at the time of the study. Neither duration of HAART nor the type of regimen influenced BMI values.” (Amorosa, 2005)

HIV Obesity trends are mirroring Global Obesity
Malnutrition

Obesity

MODERN HUMANS

Behavioral change is needed
GLOBAL Obesity Epidemic
Obesity in Latin America
Obesity in Colombia

BMI / Overweight / Obesity - prevalence - BMI ≥ 30 kg/m²
2005

<table>
<thead>
<tr>
<th>Country</th>
<th>Males</th>
<th>Females</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colombia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>United States</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Causes of Global Obesity

Environmental Influences

• Portion distortion
• Less physical activity
• Greater reliance on technology
From Ancient to Modern Diet...

From Ancient to Modern Transportation...

Why Worry?

Obesity is linked with...

• Increased risk of cardiovascular disease
• Increased risk of Diabetes
• Cancer
• Depression
What has happened in HIV?

- ARV Therapy
- Living Longer
- Survival Rates
HIGHLY ACTIVE ANTIRETROVIRAL THERAPY (HAART)

😊 Benefits

- Longer survival
- Improved quality of life

😊 Adverse effects

- Lipodystrophy syndrome
- DM2
- Alterations in glucose and lipid metabolism
- Insulin resistance
- Increase in cardiovascular risk

IDF Cape Town Report (April 2007) 10th Meeting of the Mediterranean Group for the Study of Diabetes
Lipodystrophy

• Apparent in 20-35% of patients after 12-24 months of drug therapy,
  • HIV itself
    • Subcutaneous lipoatrophy
    • Face, limbs, buttocks
    • Fat accumulation
    • Visceral
    • Dorsocervical spine (“buffalo hump”)
    • Lipomata
    • Breast enlargement

Facial Lipoatrophy

Dorsocervical Spine Fat Accumulation

Central Fat Accumulation

Limb Lipoatrophy

1992

2003
HIV-Related Metabolic Complications

- Lipid (cholesterol/triglyceride) abnormalities
- Abnormal blood sugar (glucose) metabolism
- Mitochondrial toxicity
- Body fat redistribution
- Bone

- One syndrome or several?
- One etiology or multifactorial?
### Inconsistent Results: From major studies on CVD risk in HIV-infected and HAART-treated patients

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>Event</th>
<th>ARV</th>
<th>Effect</th>
<th>Traditional risk factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>VA³</td>
<td>36,766</td>
<td>1,207 CHD</td>
<td>HAART or PI</td>
<td>No</td>
<td>Not evaluated</td>
</tr>
<tr>
<td>HOPS⁵</td>
<td>1807</td>
<td>84 CV events</td>
<td>Specific ARVs</td>
<td>No</td>
<td>Age &gt;40 y, diabetes, HTN</td>
</tr>
<tr>
<td>SMART²</td>
<td>5472</td>
<td>63 CHD</td>
<td>Intermittent HAART</td>
<td>No – stopping therapy led to complication</td>
<td>Age</td>
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<tr>
<td>Kaiser³</td>
<td>4408</td>
<td>86 MI</td>
<td>PI</td>
<td>Risk of HIV+ vs. HIV- No risk on PI</td>
<td>Not evaluated</td>
</tr>
<tr>
<td>Medi-Cal⁴</td>
<td>28,513</td>
<td>NA</td>
<td>ART</td>
<td>Risk with ART in 18–33 year olds</td>
<td>Not evaluated</td>
</tr>
<tr>
<td>DAD²</td>
<td>23,490</td>
<td>345 MI</td>
<td>cART and PI</td>
<td>Yes</td>
<td>Smoking, age, gender, HTN, DM</td>
</tr>
<tr>
<td>French⁵</td>
<td>34,976</td>
<td>49 MI</td>
<td>PI</td>
<td>Yes</td>
<td>Age</td>
</tr>
<tr>
<td>Johns Hopkins⁶</td>
<td>2671</td>
<td>Case control</td>
<td>HIV+ vs. HIV-</td>
<td>Yes</td>
<td>Age, HTN, DM</td>
</tr>
<tr>
<td>Frankfurt⁴</td>
<td>4993</td>
<td>29 MI</td>
<td>HAART</td>
<td>Yes</td>
<td>Age &gt;40</td>
</tr>
</tbody>
</table>

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2. Frits-Maler N, 13th CROI, Denver 2006, #144
8. Lichtenstein K, 13th CROI, Denver 2006, #735
Traditional factors are the biggest contributor to coronary heart disease (CHD) in HIV population.

- Gender
- Family history
- Age
- Lipids*
- Inactivity, diet
- Abdominal obesity*
- Cigarette smoking
- Hypertension*
- Hyperglycemia
- Insulin resistance*

*Metabolic syndrome

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Insulin Resistance and HIV

Classical type 2 diabetes risk factors:
- Obesity (abdominal)
- Physical inactivity
- Genetic
  - Family history
  - Race
- Older age
- Dyslipidemia

HIV-associated risk factors:
- Peripheral lipoatrophy
- Reduced adiponectin
- Increased liver or muscle fat
- Inflammatory cytokines
- Low testosterone
- Oxidant stress
- HCV infection
- PIs, NRTI’s

Venter - The New HIV Precipe? Metabolic Disorders. Reproductive Health & HIV Research Unit. University of Watersrand
MULTICENTER AIDS COHORT STUDY

Incidence of DM in HIV+ patients with HAART exposure
4 X greater than HIV-controls

- 568 HIV + men - HAART
- 710 HIV - men

Adjusted for age, BMI

- DM in HIV + rate: 4.7 cases per 100 person/yr
- DM in HIV- rate: 1.4 cases per 100 person/yr

Arch Inter Med 2005, 165: 1179

IDF Cape Town Report (April 2007)10th Meeting of the Mediterranean Group for the Study of Diabetes
DISORDERS OF GLUCOSE METABOLISM IN HIV INFECTED PATIENTS ON TREATMENT

61% of patients develop insulin resistance
14% of patients develop Metabolic Syndrome

• A collection of metabolic risk factors that accelerate the onset of:
  • diabetes,
  • heart disease,
  • stroke,
  • and certain cancers
Metabolic Syndrome

• Abdominal obesity
• Elevated TRIG
• Low HDL
• Hypertension
• Hyperglycemia

HIV Patients and risk for metabolic syndrome

Metabolic Syndrome is more prevalent in HIV-seropositive than HIV-seronegative women due to dyslipidemias. --


The prevalence of Metabolic Syndrome among HIV-infected patients is similar to that in uninfected individuals. --


Metabolic Syndrome prevalence in HIV-positive adults was lower than in the general population.

Potential Mechanisms for Metabolic Abnormalities

**Vessels**
- Increased trygliceride in circulation
- Increased apolipoprotein E
- Decreased degradation of Lipoprotein B

**Liver**
- Decreased mitochondrial fatty acid oxidation
- Increased lipid accumulation and hepatic steatosis

**Fat**
- Increased lipolysis
- Decreased subcutaneous fat
- Decreased SRBP1-activated PPAR γ expression
- Toxic effect on mitochondria

**Pancreas**
- Increased insulin secondary to resistance

**Muscle**
- Decreased glucose Transport (GLUT 4)
- Increased intramyocellular lipid and fatty acid oxidation
What Do We Know?

• Traditional lifestyle risks are most important in HIV for cardiovascular risks

• Same in diabetes
CONCLUSIONS

• Obesity is an emerging health problem among HIV+ men and women

• Metabolic and body-fat abnormalities are common among ARV treated HIV+ adults

• Preliminary evidence suggests that such patients have an increased risk of cardiovascular disease.

• Clinicians caring for HIV-infected adults should assess cardiovascular risk factors and target risk reduction, though not at the expense of successful treatment of the underlying HIV disease.

• Diet, lifestyle modification, and use of lipid-lowering and insulin-sensitizing regimens may be useful in specific situations.

• Role of intentional weight loss in obese HIV will need careful study, as weight loss is a documented predictor of decreased survival.
Acknowledgements

Victoria Elf