Lipodystrophy in HIV infected patients on long term Antiretroviral therapy in western Kenya.

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Introduction

• Changes in fat distribution has been observed in patients on highly active antiretroviral therapy.
• The frequently reported drugs that cause fat redistribution are stavudine and protease inhibitors.
• Stavudine also causes a high incidence of metabolic complications and peripheral neuropathy.
Background

• Stavudine therapy is mostly associated with lipoatrophy or loss of subcutaneous fat.
  – Prominent in the extremities and in the face
• Less commonly stavudine and protease inhibitors can cause fat accumulation syndromes
  – Abdominal obesity
  – A buffalo hump
  – Isolated breast enlargement.
Background

- HIV associated lipodystrophy is multifactorial and the leading hypothesis include:
  - Host related factors such as diet and gene mutations.
  - Viral factors such as cytokine synthesis or depletion of polyunsaturated fatty acids.
Background

• Pharmacological or drug induced
  – Mitochondrial DNA-polymerase inhibition
  – Lipolysis inhibition
  – Adiponectin (involved in lipid metabolism) synthesis reduction

• Reduced levels of adiponectin has been reported in HIV infected patients especially those receiving stavudine.
Background

• Lipodystrophy is more common in women
• Other high risk factors cited in literature include:
  – Low CD4 counts
  – Higher CDC/WHO stage
  – Low body mass index
  – High viral load
  – Previous use of other ARVs
Background

• Pattern of distribution is different in men and women
  – Men: more peripheral lipoatrophy
  – Women: mixed lipoatrophy and lipohypertrophy.
Background.

- In AMPATH clinics some patients were noted to have wasting of the extremities and face.
- Changes mainly noted by patients, family members and the clinicians.
- To describe and estimate the frequency of lipodystrophy in our setting we conducted a survey on 200 patients on long term ARV and their care providers.
Research question

• What is the pattern and frequencies of fat redistribution in a population of HIV infected patients in western Kenya, who have received at least 6 months of antiretroviral therapy?
Objectives

• To estimate the frequency of fat redistribution as perceived by the patients on ARV therapy
• To estimate the frequency of fat redistribution in those same patients as perceived by the care providers.
Methods

- Cross sectional survey of patients on ARV therapy followed up in AMPATH clinics.
- Survey instrument used was modified from the one used by the Multicenter AIDS Cohort Study (MACS) in the USA.
- Consecutive patients were recruited as they presented to the clinic.
- Research assistant asked the set of questions to both the patient and provider.
Lipodystrophy

Subject No: LP/50
Gender: Female
Current weight: 76 kg  Last CD4 count: 476/mm³
Current antiretrovirals:
- Stavudine
- Lamivudine
- Nevirapine
- Efavirenz
- Nelfinavir
- Zidovudine
- Lopinavir/ritonavir
Other:
Duration of ARV therapy: 24 mo
ARV change within the last 3 months?: NO

1a. Over the last 3 months, have you noticed any changes in the distribution or in the amount of your body fat?
- NO
- YES

1b. If yes which parts of your body were affected and how severely?

<table>
<thead>
<tr>
<th>Part of Body</th>
<th>YES</th>
<th>NO</th>
<th>Increase</th>
<th>Decrease</th>
<th>None</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Facial fat</td>
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<td>Arm fat</td>
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<td>Leg fat</td>
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<tr>
<td>Buttocks fat</td>
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<td></td>
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<tr>
<td>Abdominal fat</td>
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<tr>
<td>Back of neck fat</td>
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<td></td>
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<tr>
<td>Breasts fat</td>
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<tr>
<td>Hips</td>
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<tr>
<td>Other location</td>
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<td></td>
</tr>
</tbody>
</table>
Identify “other location”:

Record: 1 of 200
Lipodystrophy

Subject No: LP/50
Gender: Female
Current weight: 76 kg
Last CD4 count: 476 /mm
Current antiretrovirals:
- Stavudine
- Lamivudine
- Nevirapine
- Efavirenz
- Zidovudine
- Lopinavir/ritonavir
- Nelfinavir
- Other

Duration of ARV therapy: 24 mo
ARV change within the last 3 months? Yes

1. Questions for the patient
1c. Since you’ve noticed these changes, have you taken action that would influence your fat distribution such as:
- Changing diet: No
- Changing HIV medication: No
- Exercise: Yes
- Nutritional supplements: No

1d. In the last 3 months, has your clothing become:
- Too loose: No
- Too tight: Yes
- No change: No
Methods

• Inclusion criteria
  – Age 18 years or more
  – History of ARV treatment for at least 6 months
  – Willingness to answer survey questions

• Exclusion criteria
  – Lack of willingness to participate
  – Previous participation in the study.
Results

• Overall 200 patients were interviewed
• 144 (72%) were women (typical of our patient population)
• The median duration of antiretroviral therapy was 15 months (range 6-61 months)
• The median weight was 60kg (range 38-97)
Results

• Median CD4 was 265 (1-1026).
• All patients were on HAART (2 NRTIS +1NNRTI or PI).
• 55 (27.5%) patients reported change in fat distribution over the last 3 months.
• Clinicians reported that 41 (20.5%) patients had evidence of fat wasting or accumulation.
# Table 1: Patient demographics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total</th>
<th>Male (%)</th>
<th>Female (%)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total</td>
<td>N=56(28.0%)</td>
<td>N=144(72%)</td>
<td></td>
</tr>
<tr>
<td>Weight</td>
<td>Median(range)</td>
<td>60(38-97)</td>
<td>65(48-95)</td>
<td>59(38-97)</td>
</tr>
<tr>
<td>CD4 count</td>
<td>Median(Range)</td>
<td>265(1-1026)</td>
<td>216.5(1-728)</td>
<td>280(40-1026)</td>
</tr>
<tr>
<td>ARV duration in months</td>
<td>Median(Range)</td>
<td>15(6-61)</td>
<td>14.5(6-48)</td>
<td>15(6-61)</td>
</tr>
<tr>
<td>ARV change</td>
<td>Yes</td>
<td>14(7.0%)</td>
<td>3(5.36%)</td>
<td>11(7.64%)</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>186(93.0%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ARVs</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stavudine</td>
<td>181(90.5%)</td>
<td>52(92.86%)</td>
<td>129(89.58%)</td>
<td></td>
</tr>
<tr>
<td>Lamivudine</td>
<td>191(95.5%)</td>
<td>54(96.43%)</td>
<td>137(95.14%)</td>
<td></td>
</tr>
<tr>
<td>Nevirapine</td>
<td>157(78.5%)</td>
<td>42(75.00%)</td>
<td>115(79.86%)</td>
<td></td>
</tr>
<tr>
<td>Efavirenz</td>
<td>33(16.5%)</td>
<td>11(19.64%)</td>
<td>22(15.28%)</td>
<td></td>
</tr>
<tr>
<td>Zidovudine</td>
<td>15(7.5%)</td>
<td>4(7.14%)</td>
<td>11(7.64%)</td>
<td></td>
</tr>
<tr>
<td>Lopinavir_r</td>
<td>5(2.5%)</td>
<td>2(3.57%)</td>
<td>3(2.08%)</td>
<td></td>
</tr>
</tbody>
</table>
Table 2a: Changes in fat distribution (patient perceptions)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Frequency (%)</th>
<th>Male (N=56)</th>
<th>Female (N=144)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Noticed change over last 3 months</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>55(27.50%)</td>
<td>13(23.21%)</td>
<td>42(29.17%)</td>
<td>0.3973</td>
</tr>
<tr>
<td>No</td>
<td>145(72.50%)</td>
<td>43(76.79%)</td>
<td>102(70.83%)</td>
<td></td>
</tr>
<tr>
<td><strong>Changes in fat distribution</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fat accumulation (Increase)</td>
<td>43(21.50%)</td>
<td>11(19.64%)</td>
<td>32(22.22%)</td>
<td></td>
</tr>
<tr>
<td>Wasting (Decrease)</td>
<td>2(1.00%)</td>
<td>0(0.00%)</td>
<td>2(1.39%)</td>
<td></td>
</tr>
<tr>
<td>Accumulation + Wasting (Both)</td>
<td>9(4.50%)</td>
<td>2(3.57%)</td>
<td>7(4.86%)</td>
<td></td>
</tr>
<tr>
<td>No change</td>
<td>146(73.00%)</td>
<td>43(76.79%)</td>
<td>103(71.53%)</td>
<td></td>
</tr>
<tr>
<td><strong>Action taken</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>47(23.50%)</td>
<td>16(28.57%)</td>
<td>31(21.53%)</td>
<td>0.2915</td>
</tr>
<tr>
<td>No</td>
<td>153(76.50%)</td>
<td>40(71.43%)</td>
<td>113(78.47%)</td>
<td></td>
</tr>
<tr>
<td><strong>Change in clothing</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Too loose</td>
<td>16(8.21%)</td>
<td>3(5.45%)</td>
<td>13(9.29%)</td>
<td>0.5753</td>
</tr>
<tr>
<td>Too tight</td>
<td>43(22.05%)</td>
<td>11(20.00%)</td>
<td>32(22.86%)</td>
<td></td>
</tr>
<tr>
<td>No change</td>
<td>136(69.74%)</td>
<td>41(74.55%)</td>
<td>45(67.86%)</td>
<td></td>
</tr>
</tbody>
</table>
Table 2b: Changes in fat distribution (clinician’s perception)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Frequency (%)</th>
<th>Male (%) N=56(28.0%)</th>
<th>Female N=144(72%)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient exhibit changes in fat distribution</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fat accumulation (Increase)</td>
<td>29(14.50%)</td>
<td>9(16.07%)</td>
<td>20(13.89%)</td>
<td></td>
</tr>
<tr>
<td>Wasting (Decrease)</td>
<td>7(3.50%)</td>
<td>0(0.00%)</td>
<td>7(4.86%)</td>
<td></td>
</tr>
<tr>
<td>Accumulation +Wasting (Both)</td>
<td>5(2.50%)</td>
<td>0(0.00%)</td>
<td>5(3.47%)</td>
<td></td>
</tr>
<tr>
<td>No change</td>
<td>159(79.5%)</td>
<td>47(83.93%)</td>
<td>112(77.78%)</td>
<td></td>
</tr>
</tbody>
</table>
Results

• None of the risk factors such as weight, gender, CD4, type of ARV or duration of therapy were significantly related to the development of lipodystrophy in both univariate and multivariate analysis.
Conclusions

- Subjective lipodystrophy by patient or clinician survey was not uncommon.
- Since most of our patients gain weight after starting ARVs, this probably represents a minimal estimate of lipoatrophy.
- Objective measures of fat loss such as DEXA scans and CT scans may yield higher estimates.
Conclusions

• The pattern of fat redistribution may be different in our setting as compared to the USA or Europe due to:
  – Predominance of women among our cohort
  – Prevalent malnutrition
  – Heterosexual mode of HIV transmission

• More studies are needed to identify the factors that are associated with lipodystrophy in our setting.