HIV-Lipodystrophy more Prevalent in Women than Men in Tamil Nadu, India

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Abstract

Background: As antiretroviral therapy (ART) becomes more available to the HIV infected population in rural areas in India, it is important to determine the prevalence of its long term complications. Therefore, it was proposed to find out the prevalence of lipodystrophy in patients receiving ART and compare the gender differences.

Material and methods: In this cross sectional study, consenting HIV-infected patients on ART visiting Namakkal District Head Quarters Hospital, Tamil Nadu, India, were recruited. They were on generic first-line fixed dose combinations of ART. Sociodemographics, anthropometric measurements, ART regimens and duration of treatment were recorded. Patients’ self-perception of lipodystrophy was obtained using standardized questionnaires and clinically confirmed by the physician. An overnight fasting blood was drawn to determine serum lipids levels. Statistical analysis included Chi-square test, student t-test and Mann Whitney U test.

Results: There were 145 HIV-infected subjects (46.9% males, 53.1% females) receiving ART for a mean 29.4 months. Mean age of the males were 38.18 ± 8.85 and for the females, it was 33.34 ± 6.20. The mean body mass index (BMI) for the males was 21.95 ± 3.94 kg/m² while for the females it was 21.14 ± 3.54 kg/m². The overall prevalence of lipodystrophy was 60.69%; 22.72% with lipohypertrophy, 51.14% with lipoatrophy, and 22.72% with mixed pattern. Women had a higher prevalence of lipodystrophy than men (p=0.004). Lipoatrophy was higher in females (p=0.015) and mixed pattern (p=0.015). There was a higher prevalence of facial atrophy, fat loss in arms, fat loss in legs and fat loss in buttocks among women compared to men. Women with lipodystrophy had higher BMI, CD4 counts, VLDL cholesterol and triglycerides.

Conclusion: Women had significantly higher rates of generalized lipodystrophy and particularly lipoatrophy when compared with men taking first-line antiretroviral regimen. Compared with women without lipodystrophy, those with lipodystrophy had lipid abnormalities.

Keywords: Lipodystrophy, Lipoatrophy, Namakkal, India

Introduction

According to India’s National AIDS Control Organization (NACO), an estimated 2.4 million people in the country had HIV infection in 2009, 39% of them are women [1]. As of December 2010, 384726 people living with HIV are on antiretroviral therapy in India and more than 47,955 of them are in Tamil Nadu [2], India’s seventh most populous state. As ART becomes more available to the HIV infected population in Namakkal district of Tamilnadu, it is important to determine the prevalence of its long term complications. Lipodystrophy associated with long term ART has been increasingly recognized in India; lipoatrophy appears to be the predominant manifestation than lipohypertrophy [3]. Studies from the West states that women are at a higher risk of lipodystrophy than men (1.9 relative risk) [4]. Women are more likely to report fat accumulation in the abdomen and breasts and hypertriglyceridemia, whereas men are more likely to describe fat depletion from the face and extremities along with hypertension and hypercholesterolemia. Therefore, it was proposed to find out the prevalence of lipodystrophy in patients receiving ART and compare the gender differences.

Materials and Methods

Study population

In this cross sectional study, HIV-infected patients on ART, visiting the ART center at Namakkal District Head Quarters Hospital, Tamil Nadu, India, were recruited from January-April 2009. They were on generic first-line fixed dose combinations of ART (Zidovudine/Stavudine based regimens), provided for free by the Indian Government under its national ART program. All the subjects were aged 18 years or above. Written informed consent was obtained from all the participants. The exclusion criteria for all the subjects were active substance or alcohol abuse, current usage of anabolic steroids, glucocorticoids, lipid-lowering or hypoglycemic drugs, recent opportunistic infection or malignancy.

Assessments and measurements

Sociodemographic information, anthropometric measurements and details of type and duration of ART regimen were recorded. Patients’ self-perception of lipodystrophy (lipohypertrophy and lipoatrophy) was obtained using standardized questionnaires and clinically confirmed by the physician at the ART center. Lipoatrophy was defined as facial fat loss, peripheral fat loss on arms, legs or buttocks. Lipohypertrophy was defined as central fat gain on upper back, chest or abdomen. The questionnaire was administered in the local language (Tamil), which

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was spoken by all patients. The questionnaire was explained in detail to the patients to ensure all subjects understood the requirements.

Anthropometric measurements included body weight (kg), height (cm), waist circumference (cm) and hip circumference (cm). Subjects were weighed wearing light clothing and without shoes to the nearest 0.1 kg. Height was measured to the nearest millimeter using a stadiometer. Body Mass Index (BMI, weight in kg divided by the square of the height in m) was calculated. Waist circumference to the nearest millimeter was measured using a cloth tape measure halfway between the lowest rib and the iliac crest. Hip circumference to the nearest millimeter was measured at the level of the anterior superior iliac spine when this could be palpated; otherwise, it was measured at the broadest circumference below the waist. The waist-to-hip ratio (WHR) was calculated from these measures.

The CD4 counts before initiation of therapy was recorded for patients and on therapy current CD4 counts were recorded for all the HIV-infected patients. An overnight fasting blood was drawn to determine serum lipids levels. Aliquots of serum were stored at -80°C until testing. Total cholesterol, high-density lipoprotein (HDL) cholesterol, and triglycerides were analyzed by colorimetric enzymatic methods with reagents purchased from Identi (Spain) using Stat Fax 3300 chemistry analyzer (Awareness Technology, USA). Low-density lipoprotein (LDL) cholesterol and Very-density lipoprotein (VLDL) was calculated using the Friedewald formula.

**Statistical analysis**

Data was collected on an individual case basis & then translated to the SPSS version 10.0 statistics software, package for statistical analysis. Descriptive statistics were presented for all variables. Data were analyzed with the Chi-square test. Linear association between any two variables was studied using Pearson Correlation. Mean differences between the groups were analyzed by student t test and Mann Whitney U test (non parametric). A significance level of p<0.05 was used for all tests and comparisons.

**Results**

There were 145 HIV-infected subjects (46.9% males, 53.1% females) currently receiving ART for a mean 29.4 months (range, 2–60 months) (Table1). Fifty four (37.8%) of them were on generic fixed combination of AZT (zidovudine)/3TC (lamivudine) and NVP (Nevirapine) regimen while 4 (2.8%) were on AZT/3TC/EFV regimen. Eighty three (58%) subjects were on d4T (stavudine)/3TC/NVP combination while 2 (1.4%) of them were on d4T/3TC/EFV regimen. Mean age of the males were 38.18 ± 8.85 and for the females, it was 33.34 ± 6.20. The mean body mass index for the males was 21.95 ± 3.94 kg/m². The mean body mass index for the females it was 21.14 ± 3.54 kg/m². The mean CD4 count of the subjects was 143.23 μl at the initiation of antiretroviral therapy.

In this study the prevalence of self-perception of lipodystrophy was 60.7%; with 23.53% lipohypertrophy, 52.94% lipoatrophy, and 23.53% mixed pattern. There was a significant difference in the self-perception of lipodystrophy pattern between males and females with having a higher prevalence (71.4% vs 48.5%; p=0.004) (Table 2). Prevalence of lipodystrophy was also higher in females (40.8% vs 21.2%; p=0.015) as well as prevalence of mixed pattern (17.1% vs 10.6%; p=0.015). Moreover, there was also a higher prevalence of facial atrophy among women compared to men (43.4% vs 22.3%; p=0.029). Women also had a higher prevalence of fat loss in arms (34.2% vs 14.9%; p=0.025), fat loss in legs (25% vs 13.4%; p=0.210), and fat loss in buttocks (19.7% vs 4%; p=0.051). By univariate analysis, lipodystrophy was positively correlated with age (r=0.249; p=0.029) and CD4 counts (r=0.448; p=0.006) in women, but not in men.

Comparison between men and women with regard to mean CD4 counts and lipid profile values (Table 1).

**Discussion**

In this study the overall prevalence of lipodystrophy among the study subjects was 60% with more than half the patients having lipodystrophy rather than lipohypertrophy and mixed pattern. Women had significantly higher rates of generalized lipodystrophy and particularly lipodystrophy when compared with men taking first-line antiretroviral regimen at Namakkal Government Hospital in Tamil Nadu, India. Compared with women without lipodystrophy, those with lipodystrophy had significantly higher mean BMI (p=0.003), mean CD4 count (p=0.006), mean VLDL cholesterol (p=0.046) and mean triglycerides (p=0.046) (Table 3).

**Table 1:** Characteristics of participants

| Variable                  | Men n=68 | Women n=77 | P value† |
|---------------------------|----------|------------|----------|
| Age (years)               | 38.18 ± 8.85 | 33.34 ± 6.20 | 0.60     |
| Body mass index (kg/m²)   | 21.95 ± 3.94 | 21.14 ± 3.54 | 0.202    |
| Waist hip ratio           | 0.94 ± 0.09  | 0.92 ± 0.14  | 0.404    |
| ART duration (months)     | 28.67 ± 11.82 | 30.12 ± 13.79 | 0.506    |
| CD4 cell count (cells/mm³) | 140.03 ± 128.28 | 146.12 ± 113.07 | 0.766    |
| Total Cholesterol (mg/dl) | 203.43 ± 63.43 | 210.74 ± 104.74 | 0.618    |
| HDL-Cholesterol (mg/dl)   | 49.46 ± 16.41 | 55.45 ± 19.59 | 0.048    |
| LDL-Cholesterol (mg/dl)   | 118.31 ± 43.65 | 118.06 ± 99.79 | 0.985    |
| VLDL-Cholesterol (mg/dl)  | 36.39 ± 40.00 | 37.62 ± 48.32 | 0.865    |
| Triglycerides (mg/dl)     | 181.93 ± 199.78 | 188.07 ± 241.58 | 0.865    |

Table 2: Lipodystrophy pattern among men and women

| Lipodystrophy | Men (n=68) n (%) | Women (n=77) n (%) | P value† |
|---------------|------------------|-------------------|---------|
| Lipohypertrophy| 14 (21.2)        | 31 (40.8)         | 0.015   |
| Lipoatrophy   | 10 (15.2)        | 10 (13.2)         | 0.015   |
| Mixed pattern | 7(10.6)           | 13(17.1)          | 0.015   |
| Facial Atrophy| 15(22.37)        | 33(43.4)          | 0.029   |
| Fat loss in arms| 10(14.9)        | 26(34.2)          | 0.025   |
| Fat loss in legs| 9(13.4)           | 19(25)            | 0.210   |
| Fat loss in buttocks| 5(7.4)           | 15(19.7)          | 0.051   |
| Fat gain in upper back| 2 (3.0)           | 8 (10.5)         | 0.125   |
| Fat gain in chest| 3(4.5)            | 5(6.6)            | 0.432   |
| Fat gain in abdomen| 13(19.7)        | 19(25)            | 0.553   |
lipodystrophy had significantly higher CD4 counts, very low-density lipoprotein (VLDL) cholesterol, and triglycerides.

In 1998, lipodystrophy was first described while using HAART [5,6]. Several studies have recorded higher rates of lipodystrophy in women than men, including, for example, reports from Benin [7], Canada [8] and Italy [9]. Yet lipodystrophy rates clearly depend on an array of study factors, including whether the study is prospective or cross-sectional, how lipodystrophy is defined, whether objective measures are used, and the statistical methods applied. A prospective study of 245 women and 723 men in Quebec, for example, found no gender differences in the overall incidence of treatment-limiting lipodystrophy, even after statistical adjustment for age, CD4 count, viral load, time since HIV diagnosis, history of AIDS-defining illness, and year of antiretroviral initiation [10]. A recent study of 2,072 patients from 12 clinics in 12 Asian countries (including India) observed 10.5% of patients having lipodystrophy [11]. The study also found that there was an increased risk of lipodystrophy for those on ART for a longer period of time. A study from YRG care from India concluded that lipodystrophy is a predominant presentation of HIV associated lipodystrophy; however majority of the presentations was observed in males [3]. While a recent study of 32 patients on ART in South India noticed that 28% of men and 75% of women reported a change in fat distribution. Metabolic changes with increased abdominal fat and loss of peripheral subcutaneous fat especially in the face and upper limbs was more prominent in women than in men [12]. While our study findings were similar to the above observations in women with lipodystrophy, 41% of them had lipodystrophy with higher prevalence of facial atrophy, fat loss in arms, legs and buttocks. Lipodystrophy positively correlated with age in women but not in men.

Stavudine based regimens were most commonly used because of its low cost. Next to lamivudine, stavudine was the most commonly used NRTI, because of its relatively low cost [13]. Stavudine is most often associated with mitochondrial toxicity, which results in high rates of lipodystrophy, peripheral neuropathy, lactic acidosis, and pancreatitis [14]. Studies showed a higher prevalence on lipodystrophy among patients who were on Stavudine based regimens than Zidovudine even in our population [15]. This had prompted the World Health Organization to change their antiretroviral therapy policy (2006) to use zidovudine rather than stavudine. However in this study, there was no significant increase in lipodystrophy in patients receiving stavudine based regimen than zidovudine based regimens. This is contrary to other studies from India. This may be due to the small sample size in this study.

Several different techniques are available to assess fat distribution and body composition in HIV positive patients, such as DEXA, BIA, computed tomography and the use of radio-labeled water [12].

### Table 3: Comparison between women with and without lipodystrophy

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