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How Common is Lipodystrophy after > 1 year of WHO First Line Antiretroviral Treatment in Kigali, Rwanda ?

Johan van Griensven[1], Ludwig De Naeyer[1], Thomas Mushi[2], Sowaf Ubarijoro[2], Claire Gazille[1] and Rony Zachariah[1]

[1] MSF OCB, Rwanda

[2] Ministry of Health, Rwanda

MEDECINS SANS FRONTIERES

MSF-Operational Center Brussels
B.P. 1361 Kimihurura
Kigali , Rwanda
Tel: +250/510993
msfb-kigali-sida@brussels.msf.org

BACKGROUND

Current WHO guidelines recommend antiretroviral therapy (ART), including stavudine (d4T) as first line regimens in resource-limited settings. However, these have been linked with a high risk of lipodystrophy, presenting as subcutaneous (mainly peripheral) fat loss (lipoatrophy), relative or absolute accumulation of central fat (lipohypertrophy) or mixed patterns. Of these, lipoatrophy is most clearly linked with ART, especially d4T, and is most likely to improve upon treatment change. Although sub-Saharan Africa is most severely affected by the HIV pandemic, no studies have addressed the problem of lipodystrophy in an African population.

METHODS

- Since November 2003, Médecins Sans Frontières OCB is providing ART in two urban health centers in Kigali, Rwanda. By June 2006, around 2250 patients on ART were in follow-up.
- Between 0ctober 1st and April 31st, all patients on WHO first line ART regimens for > 1 year were routinely assessed for lipodystrophy. Each patient completed a Lipodystrophy Case Definition Study (LCDS)-based questionnaire and underwent a physical examination focussing on body habitus changes. Both assessments recorded independently any lipoatrophy or fat accumulation in each of the face, neck, dorsocervical spine, arms, breasts, abdomen, buttocks, and legs. The degree of lipoatrophy and fat accumulation at each region was rated using the HOPS scale: absent (score of 0), mild (noticeable on close inspection, score of 1), moderate (readily noticeable by patient/physician, score of 2) or severe (readily noticeable to a casual observer, score of 3).
- Other causes of body fat changes were excluded by clinical examination, biochemical - including CD4 cell counts and viral load - and radiological/endoscopical investigations. Given the resource-limited setting, the problem of malnutrition was specifically addressed.
- General clinical data are prospectively collected routinely in all the MSF programs. Data on lipodystrophy were first analysed with unpaired t-test and Chi-square test for numerical and categorical/binary variables respectively. Multivariate analysis for risk factors for lipoatrophy was done using a logistic regression of cases and controls (patients without body fat changes). Analysis was performed using Intercooled Stata version 9.

RESULTS

Up to date, 409 patients have been assessed for lipodystrophy (Table 1). The vast majority was taking d4T/3TC/NVP. Body fat changes were documented in 151 patients, resulting in an overall prevalence of 36.9 %. Isolated lipoatrophy was observed in 10.5 % of patients, mixed patterns in 19.6% and isolated lipohypertrophy in 7.1%. Of the 123 patients manifesting lipoatrophy, this was graded moderate to severe in 20.3 % and 49.6 % respectively (Table 1.B). Patients with fat loss had a higher baseline and maximum BMI. Lipoatrophy was associated with recent onset weight loss, occurring at a faster rate (Table 2.A). In multivariate analysis, female sex, use of d4T and longer duration of ARV were significantly associated with lipoatrophy (Table 2.B). A higher baseline BMI and CD4 cell count were additional risk factors for fat loss.

CONCLUSION

This is the first study reporting prevalence data on lipodystrophy in an African country, revealing it as a frequent complication of ART containing d4T. Simple tools to detect lipoatrophy will have to be validated in an African population. The impact of this syndrome on adherence and social stigmatization has to be assessed. These data provide additional support to advocate for affordable less toxic regimens in resource-constrained countries.

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PATIENT CHARACTERISTICS

Table 1.A. Patient characteristics (n=409)

Age†‡	39 ± 8	38 (34-44)
Sex (male/female)*	88/321 (21.5/78.5)	
Clinical stage pre-ARV*		
WHO stage I	3 (0.7)	
WHO stage II	47 (11.5)	
WHO stage III	293 (71.6)	
WHO stage IV	66 (16.2)	
BMI pre-ARV†‡	21.2 ± 3.6	20.8 (18.7-23.1)
Baseline CD4 count (cells/µL)†‡	135 ± 76	128 (74-189)
Time on ARV (months)†‡	17.6 ± 5.3	16 (13-21)
ARV regimen*		
d4T/3TC/NVP	329 (80.5)	
d4T/3TC/EFV	38 (9.3)	
AZT/3TC/NVP	26 (6.3)	
AZT/3TC/EFV	16 (3.9)	

Table 1.B. Pattern and severity of body fat changes (n=151)•

Body fat changes	151 (36.9 %)	100 %
Isolated lipoatrophy	43 (10.5 %)	28 %
Mixed pattern	80 (19.6 %)	53 %
Isolated lipohypertrophy	29 (7.1%)	19 %
Lipoatrophy∫	123 (81.5 %)	100 %
Mild lipoatrophy (score 1-3)	37 (24.5 %)	30.1 %
Moderate lipoatrophy (score 4-6)	25 (16.5 %)	20.3 %
Severe lipoatrophy (score > 6)	61 (40.5 %)	49.6 %
Lipohypertrophy∫	110 (72.8 %)	100 %
Mild lipohypertrophy (score 1- 3)	56 (37.1 %)	51.9 %
Moderate lipohypertrophy (score 3-6)	41 (27.1 %)	37.3 %
Severe lipohypertrophy (score > 6)	13 (8.6 %)	11.8 %

* Values are expressed as n (%); † Values are expressed as mean ± Standard Deviation
‡ Values are expressed as median (interquartile range); ∫ A total score was obtained by adding the scores for each body region. A total score of 1-3 was (arbitrarily) defined as mild, a score > 6 was considered severe.

ANALYSIS OF RISK FACTORS FOR LIPOATROPHY

Table 2.A. Characteristics of patients with and without lipoatrophy

	Lipoatrophy (n=123)	No changes (n=258)	P value
Age†	39 ± 7	39 ± 8	0.991
Sex (male/female)‡	10/113 (8.1/91.9)	76/181 (29.6/70.4)	0.000*
ART regimen (D4T/AZT)‡	118/5 (96/4)	226/31 (88/12)	0.013*
Clinical stage pre-ARV‡			
WHO stage I	1 (0.8)	1 (0.4)	0.784
WHO stage II	16 (13.0)	29 (11.3)	
WHO stage III	89 (72.4)	183 (71.2)	
WHO stage IV	17 (13.8)	44 (17.1)	
BMI pre-ARV†	22.2 ± 3.9	20.8 ± 3.2	0.000*
BMI maximal (max)†	23.9 ± 4.0	22.3 ± 3.5	0.000*
BMI current†	22.3 ± 3.4	22.0 ± 3.3	0.495
BMI increase (max - pre-ARV)†	1.7 ± 1.5	1.6 ± 2.2	0.583
BMI decrease (current - max)†	1.6 ± 1.6	0.3 ± 0.6	0.000*
Time of weight loss (kg/wk)†	0.51 ± 0.36	0.20 ± 0.15	0.000*
CD4 count pre-ARV (cells/µL)†	149 ± 81	131 ± 74	0.030*
CD4 count maximal (cells/µL)†	533 ± 156	296 ± 154	0.026*
CD4 count increase (6 months)†	113 ± 91	112 ± 96	0.906
CD4 count current†	309 ± 154	279 ± 153	0.083
Time on ARV (months)†	18.4 ± 5.3	17.2 ± 5.2	0.030*

Table 2.B. Analysis of risk factors for lipoatrophy

	Univariate analysis		Multivariate analysis	
Risk factor	OR (95% CI)	P-value	OR (95% CI)	P-value
d4T use	3.24 (1.21-8.62)	0.013	4.46 (1.33-14.91)	0.015*
Female sex	4.74 (2.30-9.77)	0.000	4.36 (1.92-9.91)	0.000*
Baseline BMI > 25 kg/m²	2.83 (1.49-5.37)	0.001	2.42 (1.25-4.68)	0.008*
Baseline CD4 cell count∫	1.41 (0.99-1.32)	0.071	1.21 (1.02-1.44)	0.029*
Time on ARVF	1.55 (1.13-2.13)	0.006	1.83 (1.23-2.72)	0.003*
Age (per additional 10 year)	0.97 (0.74-1.26)	0.801	1.12 (0.79-1.58)	0.504

† Values are expressed as mean ± Standard Deviation; ‡ Values are expressed as n (%); * P-value < 0.05
F per additional 6 months; ∫ per increment of 50 cells/µl