

Prevalence of lipodystrophy and metabolic syndrome at the bertoua day hospital (east region of Cameroon)

Abstract

This cross-sectional study, carried out on a cohort of 568 HIV-infected patients followed at the Bertoua Day Hospital, aimed at assessing interventions used in the biomedical management of lipodystrophy and metabolic syndrome related to Antiretroviral therapy through the determination of their prevalence within this hospital. Patients had a minimum age of 18 years old, a minimum duration of 2 years antiretroviral therapy and all had given their informed consent to participate in the study. The mean duration of treatment for HIV patients with lipodystrophy cases was 68 ± 9.2 months ranged from 24 to 136 months and that for patients with metabolic syndrome cases was 46 ± 8.5 months ranged from 24 to 151 months (P value = 0.005). Lipodystrophy was observed with all the therapeutic protocols prescribed to HIV-infected patients in our study site. Lipodystrophy cases seen among HIV-infected patients using the d4T in their therapeutic protocol accounted for 41.11%, while those seen among HIV-infected patients using the AZT in their therapeutic protocol accounted for 51.57% ($P < 0.0001$). Among HIV-infected patients using the NVP in their therapeutic protocol, we found 40.41% of lipodystrophy cases versus 28.23% of lipodystrophy cases among HIV-infected patients using the EFV in their therapeutic protocol (P value = 0.01). Lipodystrophy cases related to the use of protease inhibitors in the therapeutic protocol accounted for 31.36%. The prevalence of metabolic syndrome cases was greatest among HIV-infected patients using protease inhibitors boosted by the ritonavir in their therapeutic protocol with 72.6% of cases (P value = 0.0003). The prevalence of metabolic syndrome cases determined in this study using the definition of the National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP III) was 21.83% and that of lipodystrophy cases was 50.52% with 27.64% for lipodystrophy cases, 20.95% for lipohypertrophy cases and 1.93% for mixed syndrome cases (P value = 0.01). We also found 16.9% for lipodystrophy cases strongly associated with the metabolic syndrome among our HIV infected patients under HAART, with an Odds Ratio of 4.54 which was statistically significant with a confidence interval (CI) between 3.45 and 6.87 to 95% (P value = 0.03). In other words, these HIV infected patients were 4.54 times more likely to have a metabolic syndrome in the presence of lipodystrophy than in its absence.

Keywords: lipodystrophy, metabolic syndrome, prevalence, haart, hiv infected patient

Volume 4 Issue 4 - 2017

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Received: April 04, 2017 | **Published:** April 24, 2017

Abbreviations: CI, confidence interval; HAART, highly active antiretroviral therapies; HIV, human immunodeficiency virus; PI, protease inhibitors; RTI, reverse transcriptase inhibitors; BMI, body mass index; NRTI, nucleotide reverse transcriptase inhibitors

Introduction

The use of highly active antiretroviral therapies (HAART) has reduced the mortality and morbidity associated with the Human Immunodeficiency Virus (HIV) infection.¹ However, these treatments are associated with long term complications as the lipodystrophy syndrome, metabolic syndrome, diabetes mellitus, lactic acidosis etc.² Among these complications, the lipodystrophy syndrome is often very remarkable. The unattractive nature of lipodystrophy can lead to self-stigmatization, stigmatization, marginalization and even reduced compliance in patients on treatment.^{3,4} The morphological and metabolic complications associated with the long-term use of HAART have been widely described in developed countries. In these countries, lipodystrophy syndrome has a prevalence ranging between 20 and 80% according to the studies.⁵ In the Aquitaine cohort in France, 38% of patients showed signs of lipodystrophy syndrome, including 16% for the lipodystrophy, 12% for the lipohypertrophy and 10% for the mixed syndrome.⁶ In sub-Saharan Africa, a Rwandan

study estimated the prevalence of lipodystrophy syndrome at 34%.⁷ There is currently no precise definition of lipodystrophy syndrome, which in part explains the difference in prevalence between studies. Protease inhibitors (PI) and reverse transcriptase inhibitors (RTI), particularly the Stavudine, are the most implicated in the occurrence of morphological and metabolic abnormalities.⁸

The abnormal fat distribution in the body observed in the lipodystrophy syndrome is at the origin of the metabolic syndrome. Its prevalence, found in some studies made on it, is very dependent on the definition used. In France, this prevalence is estimated to 10% according to the American criteria of NCEP-ATP III (National Cholesterol Education Program Adult Treatment Panel III) from 2005.⁹ In Africa, Eholié in the Lipo-Afri study estimated the prevalence of the metabolic syndrome at 17.8%.¹⁰ The occurrence of metabolic disorders among HIV-infected patients under HAART should consider their follow-up among HIV-infected patients because of the potential risk for cardiovascular, liver and diabetes complications. Hence the purpose of this study carried out on a cohort of HIV-infected patients followed at the Bertoua Day Hospital, in order to appreciate the interventions used in the biomedical follow-up for lipodystrophy and metabolic syndromes linked to HAART through the determination of their prevalence within that hospital.

Materials and methods

Study design, sampling and population

We performed a cross-sectional stud with retrospective and prospective data collection from 05th November 2015 to 08th September 2016, on a cohort of 568 HIV-infected patients under HAART followed at the Bertoua Day Hospital. We performed a simple random sampling. Patient recruitment was carried out progressively at the time of their medical follow-up.

Inclusion criteria and exclusion

We included all patients infected with HIV-1 and/or 2, with at least two years old of antiretroviral therapy, with a minimum age of 18 years old and who have given their informed consent to participate in the study. We excluded from our study all patients with pregnancy; Renal, hepatic or cardiovascular diseases.

Therapeutic protocol

The therapeutic protocol of our HIV-infected patients consisted of 2 NRTI + 1 NNRTI or 2 NRTI + 1 IP/ r (Table 1 & Figure 1) and the mean duration for treatment of these patients was 4 years (48 months).

Table 1 Distribution of lipodystrophy types according to the therapeutic protocol

| Therapeutic Protocol | Lipoatrophy | Lipohypertrophy | Mixed Syndrome | Total |
|----------------------|-------------|-----------------|----------------|------------|
| d4T-3TC-NVP | 23(14.65%) | 18(15.13%) | 4(36.37%) | 45(15.68%) |
| AZT-3TC-NVP | 56(35.67%) | 12(10.08%) | 3(27.27%) | 71(24.73%) |
| AZT-3TC-EFV | 26(16.57%) | 14(11.77%) | 1(9.09%) | 41(14.3%) |
| d4T-3TC-EFV | 14(8.91%) | 26(21.85%) | 0 | 40(13.93%) |
| d4T 3TC LPV/r | 12(7.65%) | 19(15.96%) | 2(18.18%) | 33(11.5%) |
| AZT-3TC-LPV/r | 7(4.46%) | 16(13.44%) | 1(9.09%) | 24(8.36%) |
| AZT-3TC-IDV/r | 5(3.18%) | 7(5.89%) | 0 | 12(4.18%) |
| ABC-DDI-LPV/r | 8(5.09%) | 5(4.2%) | 0 | 13(4.54%) |
| ABC-TDF-LPV/r | 6(3.82%) | 2(1.68%) | 0 | 8(2.78%) |
| Total | 157(54.7%) | 119(41.47%) | 11(3.83%) | 287(100%) |

The Percentages difference was statistically significant with a P value=0.0005.

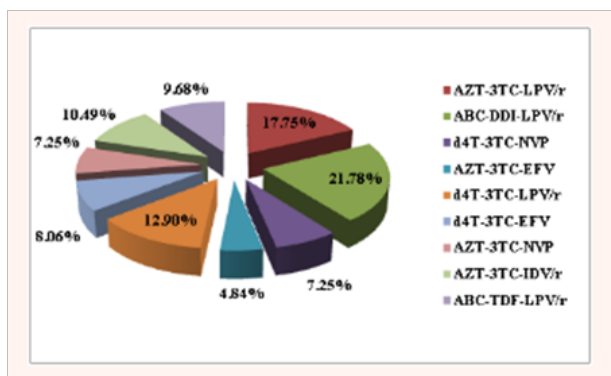


Figure 1 Prevalence of metabolic syndrome cases according to the therapeutic protocol.

Collection of data

It was done randomly in our place of study. We collected socio-demographic variables (age, sex), anthropometric variables (weight, height and waist), clinical variables (morphological variations and their perception since the beginning of HAART / lipodystrophy research), immunological variables and Virological (HIV type, CD4 count,

viral load), Biochemical variables (total cholesterol, triglycerides, HDL-cholesterol, LDL-cholesterol, Blood sugar), Treatment-related variables (therapeutic protocol, duration of treatment). The data collection about the metabolic syndrome was done by focusing on the definition of the National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP III).

Statistical analysis

The data collected were analyzed using the version 2.13 of R software and Excel software. Chi-square and Fisher statistical tests were used to compare the different percentages of the variables studied with a significance threshold set at 5%.

Ethical Consideration

Participation in the study was voluntary after being verbally informed about the objectives and constraints of the study. The confidentiality of participants was preserved throughout the study period and was not published.

Results

During our study period, we took a census of 568 participants (HIV-infected Patients) who were following their antiretroviral therapy at the Bertoua Day Hospital with a sex ratio of 0.67 in favor of the women who represented 59.85% of the participants in our study. Among these 568 participants, we identified 287 lipodystrophy cases, 124 cases for metabolic syndrome and 96 lipodystrophy cases associated with the metabolic syndrome with respective prevalences of 50.52%, 21.83% and 16.9%. The prevalences of lipoatrophy cases, lipohypertrophy cases and mixed syndrome cases were 27.64%, 20.95% and 1.93%, respectively.

The lipodystrophy syndrome

Demographic and anthropometric characteristics of HIV-infected patients with lipodystrophy

Age: The mean age of HIV infected patients with lipodystrophy was 40±6.4 years ranged from 18 to 72 years old. The age group of 50 years old and above had the highest percentages of lipoatrophy cases and lipohypertrophy cases with 53.5% and 43.7% respectively (Table 2).

Gender: The sex-ratio was 0.6 in favor of women which accounted for the highest percentage of lipodystrophy cases with 62.37% (Table 3).

Body mass index (BMI): mean of BMI for HIV-infected patients with lipodystrophy was 25±8.6kg/m². The lipoatrophy cases were more represented among patients with BMI≤18.5 kg/m² with a rate of 47.13% (Table 4).

Characteristics related to HIV infection

Therapeutic protocol: Lipodystrophy cases observed among HIV-infected patients using a therapeutic protocol including the d4T accounted for 41.11%, while those observed among HIV-infected patients using a therapeutic protocol including the AZT accounted for 51.57% (P<0.0001). Among HIV-infected patients using the NVP in their therapeutic protocol, we found 40.41% of lipodystrophy cases versus 28.23% of lipodystrophy cases among patients using the EFV in their therapeutic protocol (P value= 0.01). The cases of lipodystrophy related to the use of protease inhibitors in the therapeutic regimen accounted for 31.36% (Table 1).

The duration of HAART: The mean duration of HAART was 68±9.2

months ranged from 24 to 136 months. We also noticed cohesion between the duration of antiretroviral therapy and the increasing percentages of lipodystrophy cases recorded during our study period (Table 5).

The Percentages difference was statistically significant with a P value= 0.001.

Table 2 Distribution of HIV-infected patients with lipodystrophy according to the age group and type of lipodystrophy

| Age Group (In Year Old) | Lipoatrophy | Lipohypertrophy | Mixed Syndrome | Total |
|-------------------------|-------------|-----------------|----------------|-------------|
| 18 to 30 | 5(3.19%) | 8(6.72%) | 0 | 13(4.53%) |
| 30 to 40 | 22(14.01%) | 28(23.53%) | 2(18.18%) | 52(18.11%) |
| 40 to 50 | 46(29.3%) | 31(26.05%) | 6(54.55%) | 83(28.93%) |
| 50 and above | 84(53.5%) | 52(43.7%) | 3(27.27%) | 139(48.43%) |
| Total | 157(54.7%) | 119(41.47%) | 11(3.83%) | 287(100%) |

The percentages difference was statistically significant with a P value= 15.74×10^{-5} .

Table 3 Distribution of HIV-infected Patients with lipodystrophy according to the gender and type of lipodystrophy

| Gender | Lipoatrophy | Lipohypertrophy | Mixed Syndrome | Total |
|--------|-------------|-----------------|----------------|-----------|
| Male | 108(37.63%) | 65(41.4%) | 40(33.6%) | 3(27.27%) |
| Female | 179(62.37%) | 92(58.6%) | 79(66.4%) | 8(72.73%) |
| Total | 287(100%) | 157(54.7%) | 119(41.47%) | 11(3.83%) |

The percentages difference was statistically significant with a P value= 0.03.

Table 4 Distribution of HIV-infected patients with lipodystrophy according to BMI and type of lipodystrophy

| BMI (kg/m ²) | Lipoatrophy | Lipohypertrophy | Mixed Syndrome | Total |
|--------------------------|-------------|-----------------|----------------|------------|
| ≤18.5 | 74(47.13%) | 0 | 0 | 74(25.79%) |
| [18.5-25] | 44(28.02%) | 26(21.85%) | 1(9.09%) | 71(24.73%) |
| [25-30] | 29(18.48%) | 55(46.22%) | 3(27.28%) | 87(30.31%) |
| >30 | 10(6.37%) | 38(31.93%) | 7(63.63%) | 55(19.17%) |
| Total | 157(54.7%) | 119(41.47%) | 11(3.83%) | 287(100%) |

The percentages difference was statistically significant with a Pvalue= 1.87×10^{-8} .

Table 5 Distribution of HIV-infected patients with lipodystrophy according to the duration of HAART and type of lipodystrophy

| HAART Duration (In months) | Lipoatrophy | Lipohypertrophy | Mixed Syndrome | Total |
|----------------------------|-------------|-----------------|----------------|------------|
| [24-36] | 9(5.73%) | 3(2.53%) | 0 | 12(4.18%) |
| [36-48] | 20(12.74%) | 7(5.88%) | 1(9.09%) | 28(9.76%) |
| [48-60] | 26(16.57%) | 21(17.65%) | 1(9.09%) | 48(16.72%) |
| [60-72] | 29(18.47%) | 23(19.32%) | 3(27.28%) | 55(19.16%) |
| [72-84] | 31(19.74%) | 29(24.37%) | 2(18.18%) | 62(21.6%) |
| ≥84 | 42(26.75%) | 36(30.25%) | 4(36.36%) | 82(28.58%) |
| Total | 157(54.7%) | 119(41.47%) | 11(3.83%) | 287(100%) |

Table 6 Prevalence of metabolic syndrome types diagnosed in our study population

| Type of Metabolic Syndrome | Percentages | Prevalences |
|--|-------------|-------------|
| Abdominal Obesity + Hyperglycemia + HypoHDLemia | 15.32% | 3.35% |
| Abdominal Obesity + HypoHDLemia + Hypertriglyceridaemia | 17.75% | 3.88% |
| Abdominal Obesity + Hypertriglyceridaemia + hypertension | 12.90% | 2.81% |
| Abdominal Obesity + Hyperglycemia + HypoHDLemia + hypertension | 9.68% | 2.11% |
| Abdominal Obesity + HypoHDLemia + Hypertriglyceridaemia + hypertension | 12.09% | 2.64% |
| Abdominal Obesity + Hypertriglyceridaemia + hypertension | 10.48% | 2.29% |
| HypoHDLemia + Hypertriglyceridaemia + Hyperglycemia | 7.26% | 1.59% |
| HypoHDLemia + Hyperglycaemia + hypertension | 4.84% | 1.05% |
| HypoHDLemia + hypertriglyceridemia + hypertension | 2.42% | 0.53% |
| Hypertriglyceridaemia + Hyperglycaemia + hypertension | 5.64% | 1.23% |
| HypoHDLemia + Hypertriglyceridaemia + Hyperglycemia + hypertension | 1.62% | 0.35% |
| Total | 100% | 21.83% |

The difference in rates was not statistically significant with a Pvalue=0.36.

Table 7 Distribution of HIV-infected patients according to the lipodystrophy associated with the metabolic syndrome

| Metabolic Syndrome | OR (CI to 95%) | P value | |
|--------------------|----------------|------------------------|-----------------|
| | | Yes | No |
| Lipodystrophy | Yes | 287(50.52%) (33.4%) | 191 (66.6%) |
| | No | 281(49.48%) (9.96%) | 253 (90.04%) |
| | | 4.54 (3.45-6.87) 0.03 | |

CI, confidence interval; OR, odds ratio.

Table 8 Distribution of HIV-infected patients according to the types of lipodystrophy associated with the mixed syndrome

Mixed Syndrome

| Types of lipodystrophy | Yes | No | OR (CI to 95%) | P Value |
|------------------------|-----|-------------|----------------|---------|
| Lipohypertrophy | Yes | 119 64 55 | 2.09 | 0.01 |
| | No | 168 60 108 | (1.06-3.58) | |
| Lipoatrophy | Yes | 157 23 134 | 0.04 | 0.001 |
| | No | 130 101 29 | (-0.9 -1.53) | |
| Mixed Syndrome | Yes | 11 9 2 | 6.49 | 0.04 |
| | No | 276 113 163 | (5.46-7.98) | |

CI, confidence interval; OR, odds ratio.

Morphological modifications

Lipodystrophy localization: In a same HIV-infected patient we could notice several lipodystrophy localizations. But, the abdomen was the most frequent localization with 43.21% of cases, followed by the buttocks with 22.99%. The Percentages difference was statistically significant with a P value= 0.05 (Figure 2).

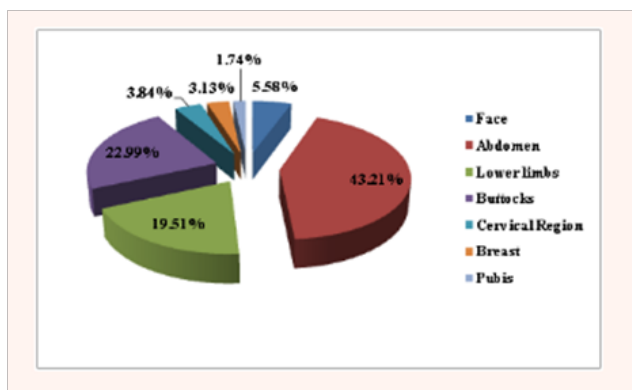


Figure 2 Distribution of HIV-infected patients according to the lipodystrophy localization.

The metabolic syndrome

Demographic and anthropometric characteristics of Metabolic Syndrome

Age: The prevalence of metabolic syndrome cases increased with age. The mean age was 42 ± 8.6 years old ranged from 18 to 72 years old. The age group of 50 and above was the most represented with 41.51% metabolic syndrome cases. The percentages difference was statistically significant with a P value= 0.04 (Figure 3).

Gender: The sex ratio was 0.58 in favor of women which accounted for the highest percentage of metabolic syndrome cases with 63%

(Figure 4). The percentage difference was statistically significant with a P value = 0.01.

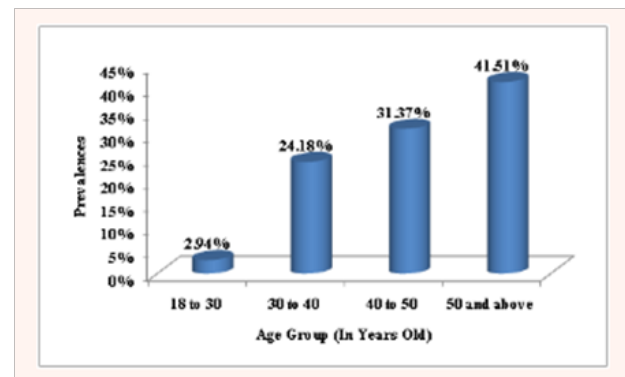


Figure 3 Prevalence of metabolic syndrome according to the age group.

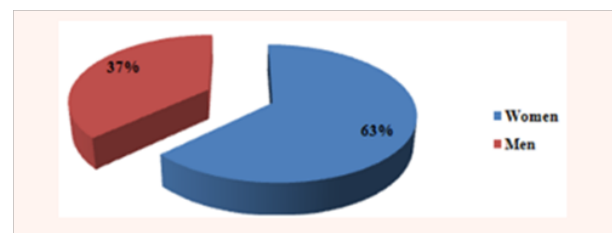


Figure 4 Prevalence of metabolic syndrome cases according to the gender.

Body mass index (BMI) : The mean of BMI was $28.32 \pm 5.7 \text{ Kg/m}^2$. The prevalence of metabolic syndrome cases was higher in the BMI range from 25 to 30 Kg/m^2 with 48.36% (Figure 5). The percentages difference was not statistically significant with a P value= 0.54.

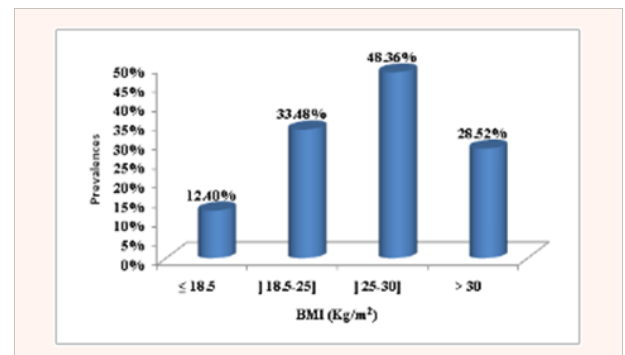


Figure 5 Prevalence of metabolic syndrome cases according to the Body Mass Index.

Therapeutic aspect of the metabolic syndrome

Therapeutic protocol: The prevalence of metabolic syndrome cases was higher among HIV-infected patients using the protease inhibitors boosted by the ritonavir (Figure 1). The percentage difference was statistically significant with a P value=0.0003.

The duration of HAART: The prevalence of metabolic syndrome cases also increased with the HAART duration. The mean HAART duration was 46 ± 8.5 months ranged from 24 to 151 months. The prevalence of metabolic syndrome cases was higher among HIV-infected patients with HAART duration ≥ 84 months (Figure 6). The percentages difference was statistically significant with a P value=0.005.

Type of Metabolic Syndrome: The metabolic syndrome with

abdominal obesity was the most represented among our HIV-infected patients with 78.2% and a general prevalence of 17.07% (Table 6).

Lipodystrophy and metabolic syndrome

Among the 287 HIV-infected patients with lipodystrophy, 96(33.4%) had a metabolic syndrome (Table 7). We found a strong association between lipodystrophy and metabolic syndrome in our HIV-infected patients with an Odds Ratio = 4.54 which was statistically significant with a confidence interval (CI) between 3.45 and 6.87 to 95% and P value= 0.03.

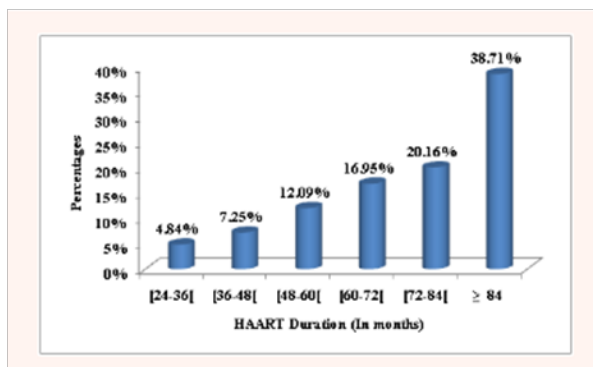


Figure 6 Prevalence of metabolic syndrome cases according to HAART duration.

Types of lipodystrophy associated with the metabolic syndrome : By focusing our attention on types of lipodystrophy, we found that lipohypertrophy and mixed syndrome were strongly associated with the metabolic syndrome with an Odds Ratio of 2.09 and 6.49 respectively. These Odds Ratio were all statistically significant (Table 8).

Discussion

Prevalence

Our study reports a prevalence of 50.52% of lipodystrophy cases; with 27.64% of lipoatrophy cases, 20.95% of lipohypertrophy cases and 1.93% of mixed syndrome cases. This prevalence of lipodystrophy cases varies from one study to another. In Rwanda, Mutimura found a prevalence of 34%.⁷ Mercier in Senegal¹¹ and Zannou in Benin¹² found prevalences of 31.1% and 30%, respectively. In the Aquitaine cohort in France,¹³ 38% of HIV-infected patients showed lipodystrophy signs, including 16% for lipoatrophy cases, 12% for lipohypertrophy cases and 10% for mixed syndrome cases. Pujari in India [8] found a prevalence of 46.1%. Miller in Australia found a prevalence of 53% for lipodystrophy cases, with 31% for lipoatrophy cases, 14% for lipohypertrophy and 55 % for mixed syndrome.¹⁴ This prevalence difference is partly due to the fact that there is currently no consensual definition of lipodystrophy but also to the variety of therapeutic protocols used and the duration of exposure to antiretroviral drugs.¹⁵

The prevalence of metabolic syndrome cases in our study was 21.83% according to the definition of NCEP-ATP III. It is higher than that found in studies made by Sawadogo in Burkina Faso,¹⁶ Jerico in Spain¹⁷ and Biron in France,¹⁸ who found prevalences of 14%, 17% and 19.9% respectively with the same definition of the metabolic syndrome used in our study. Eholié in the Lipo-Afri study reported a prevalence of 17.8% with the IDF definition.¹⁰ Indeed, the prevalence of the metabolic syndrome is highly dependent on the definition used. However, the difference in the results obtained with the same definition criteria in our study (NCEP-ATP III) also seems to be

related to the nature of the therapeutic protocols used and the duration of exposure to antiretroviral drugs.

We also found 16.9% of lipodystrophy cases strongly associated with the metabolic syndrome among our HIV patients under HAART, with an Odds Ratio of 4.54 which was statistically significant and a confidence interval (CI) between 3.45 and 6.87 to 95%. In other words, these HIV-infected patients were 4.54 times more likely to have a metabolic syndrome in the presence of lipodystrophy than in its absence (Table 7). By focusing our attention on the types of lipodystrophy, we found that lipohypertrophy and mixed syndrome were strongly associated with the metabolic syndrome with statistically significant Odds Ratio of 2.09 and 6.49 respectively (Table 8). Under HAART, our HIV-infected patients with lipohypertrophy were 2.09 times more likely to have a metabolic syndrome and those with mixed syndrome were 6.49 times more likely to have metabolic syndrome. This observation was also made by Thiébaud and Zannou in their study with the definition of the IDF.^{6,12} The literature reports that dyslipidemias are associated but not always with lipodystrophy among HIV-infected patients under HAART.^{9,2,15,19}

Age

The mean age of HIV-infected patients with lipodystrophy was 40±6.4 years old ranged from 18 to 72 years old. The age group of 50 years and above had the highest percentages of lipoatrophy cases and lipohypertrophy cases with 53.5% and 43.7% respectively (Table 2). Older age would be predisposing to lipodystrophy among the HIV-infected patient under HAART. This finding is similar to the results of many other studies about lipodystrophy among HIV-infected patients under HAART.^{6,7,8,12}

The mean age of HIV-infected patients with the metabolic syndrome cases under HAART was 42±8.6 years old ranged from 18 to 72 years old. The age group of 50 and above was also the most represented with 41.51% of metabolic syndrome cases (Figure 3). This finding in our study reflects the fact that the prevalence of the metabolic syndrome increases with age. Eholié and Jerico made the same observation in their studies.^{10,17} Ageing would be a predisposing factor to the metabolic syndrome among HIV-infected patients under HAART. Studies have shown that HIV-infected patients have the same complications related to the ageing (dyslipidemia, diabetes and insulin resistance) 10-15 years earlier than the general population.^{19,20}

Sex

The sex-ratio was 0.67 in favor of women who represented 59.85% of participants in our study. This could be explained by the fact that the follow-up for the antiretroviral therapy is more regular among women than among men because of their body physiology. This finding was also made by Marcellin in his study about the Nutritional State Impact on Liver Detoxification Function among Infected Patients with HIV under Antiretroviral Drugs^{21,22} in the same study site. This difference in body physiology could also explain the large percentage of lipodystrophy cases (62.37%) found among women in our study (Table 3). This finding was confirmed by Galli in his study about the Gender differences in antiretroviral drug related adipose tissue alterations.²³

The prevalence of the metabolic syndrome was also higher in women with 63% versus 37% in men (Figure 4). This result is similar to the one reported in the studies made by Zannou and Samaras.^{12,24} This result is also confirmed in Galli's study, which reports that hypertrophy of visceral adipose tissue is more common among women than among men.²⁵

The body mass index (BMI)

The mean of BMI among HIV-infected patients with lipodystrophy was $25 \pm 8.6 \text{ kg/m}^2$. We found that lipoatrophy was more represented among HIV-infected patients with $\text{BMI} \leq 18.5 \text{ kg/m}^2$ with 47.13% (Table 4). This finding is somewhat distant from those made by Griensven in Rwanda in his study about the prevalence of lipoatrophy among HIV-infected patients under 1st line of the antiretroviral therapy and by Thiébaud in the Aquitaine cohort in France.^{6,25}

The hypothesis of changes in the volume of body fat (loss or accumulation) that influence the weight and the BMI value can give an explanation for this finding made in our study. Young in his study about the Body fat changes among antiretroviral-naïve patients on PI and NNRTI-based HAART in the Swiss HIV Cohort Study, showed the relationship between volume changes of body fat and BMI.²⁶

The average of BMI among HIV-infected patients with the metabolic syndrome was $28.32 \pm 5.7 \text{ kg/m}^2$. The prevalence of these metabolic syndrome cases was higher in the BMI ranged from 26 to 30 kg/m^2 with 48.36% (Figure 5). Our results corroborate with those found in studies made by Eholié, Biron and Jerico.^{10,17,18} The hypertrophy of the adipose tissue or the accumulation of fat in particular visceral being a key element in the definition of the metabolic syndrome, according to the criteria of the NCEP-ATP III could still explain our results.

The therapeutic protocol

Lipodystrophy was observed with all therapeutic protocols prescribed in our study site for HIV-infected patients. AZT and d4T belonging to the class of NRTI, incriminated in the occurrence of lipodystrophy,²⁷ were found in the therapeutic protocol of patients with lipodystrophy in 51.57% and 41.11% of cases respectively ($P < 0.0001$). Lipoatrophy cases were more represented among our HIV-infected patients treated with NRTI (d4T or AZT) with 75.8% compared to 58.85% of lipohypertrophy cases (Table 1). This percentages difference was statistically significant with a P value = 0.01 and this finding is justified in the literature review which highlights the toxic effect of nucleotide reverse transcriptase inhibitors (NRTI) on the mitochondrial DNA γ polymerase which inhibits the functioning of the cellular respiratory chain and inhibits the oxidation pathways of fatty acids (dysfunction of adipose cells), hence the appearance of subcutaneous lipoatrophy.^{28,29} Griensven in his study about the prevalence of lipoatrophy made the same observation as us; 31.4% of HIV-infected patients with d4T had lipoatrophy ($p = 0.019$).²⁵ Similarly, Mercier in his study showed that exposure to d4T greater than 6 months was significantly associated with lipodystrophy ($p = 0.004$). Pujari in his study found a significant association between the use of d4T and the occurrence of lipoatrophy ($p = 0.04$) and no association between the use of therapeutic protocol such as AZT-3TC-NVP, D4T-3TC-NVP and the occurrence of lipodystrophy.⁸

The cases of lipodystrophy related to the use of protease inhibitors in the therapeutic protocol accounted for 31.36% (Table 1). Our proportion is somewhat lower than the 37% reported by Thiébaud⁶ and the 43.9% reported by Eholié in the Lipo-Afri study.¹⁰ Studies have shown a significant association between the use of protease inhibitors and lipodystrophy among HIV-infected patients.^{6,14,30} Indeed, the relationship between protease inhibitors and lipodystrophy is known. Protease inhibitors would lead to oxidative stress and hypertrophy of adipose tissue.^{31,32}

Among HIV-infected patients using the NVP in their therapeutic protocol, we found 40.41% of lipodystrophy cases versus 28.23% of

lipodystrophy cases among HIV-infected patients using the EFV in their therapeutic protocol with P value = 0.01 (Table 1). This finding is similar to the one made by Mutimura who found in his study that the use of the EFV was associated with a lower prevalence of lipodystrophy cases than the NVP, that is 15.4%.⁷ Indeed, previous studies that have addressed the issue of NNRTI and their relationship to lipodystrophy have concluded that NNRTI have more favorable effects on the redistribution of fat mass.^{11,33} Concerning the metabolic syndrome, its prevalence was higher among HIV-infected patients using protease inhibitors boosted by the ritonavir with 82.28% of cases (Figure 6). Our results are similar to those found by Thiébaud, Eholié & Jerico.^{6,10,17,34} Indeed, it is recognized that the majority of Protease inhibitors disrupt lipid parameters and lead to elevated triglycerides, total cholesterol and LDL-cholesterol, as well as an increase of the blood sugar level and insulinaemia, but to different degrees.^{2,15,35,36}

Duration of exposure to antiretroviral therapy

The mean duration of the antiretroviral therapy for HIV-infected patients with lipodystrophy was 68 ± 9.2 months ranged from 24 to 136 months. We also found a cohesion between the duration of the antiretroviral therapy and the increasing percentages of lipodystrophy cases recorded during our study period (Table 5). Our finding is similar to that found in a large number of lipodystrophy study that also found that long exposure to HAART was associated with lipodystrophy.^{6,14,25,30,36,37} The finding evoked in our study could be explained in the literature review which reports that the toxicity of some ARV drugs induces a mitochondrial dysfunction and an oxidative stress that are at the origin of the occurrence of the lipodystrophy syndrome.^{31,37} As a result, long exposure to these molecules would promote the occurrence of this dysfunction.

The prevalence of the metabolic syndrome cases also increased with duration of the antiretroviral therapy. The mean duration of the antiretroviral therapy for our HIV-infected patients under HAART was 46 ± 8.5 months ranged from 24 to 151 months. The prevalence of metabolic syndrome cases was higher among patients with therapy duration ≥ 84 months (Figure 6). Our finding is similar to the one made by Thiébaud in the Aquitaine cohort in France despite the difference in duration of exposure to antiretroviral therapy.⁶ Our results can be explained with the role played by ARV drugs in the occurrence of metabolic disorders that appear in the long term during the exposure period.

Localization of the lipodystrophy

In a same HIV-infected patient we could notice several localizations of the lipodystrophy. But the abdomen was the most frequent localization with 43.21% of cases, followed by the buttocks with 22.99%. (Figure 2). Our finding, despite the difference in percentage, is similar to those made by Mutimura and Thiébaud, who also found that the abdomen was most affected by lipodystrophy compared to other parts of the body, respectively in 84% and 20.7% of cases.^{6,7} The high consumption of alcohol and fatty food found among our HIV-infected patients under HAART could justify this finding made in our study.

Limitations of the study

Scientific honesty allows us to admit that this study was not perfect, and thus, its limits should be precised. The prevalences found in our study don't really extend to the whole of Bertoua city (East Region of Cameroon), because of the difficulties of regular follow-up for HIV-infected patients under HAART namely: loss of view, transfer, abandonment of antiretroviral therapy and deaths.

Conclusion

Our study, despite its limitations, reports a prevalence of 27.64% of lipodystrophy cases, 20.95% of lipohypertrophy cases and 1.93% of mixed syndrome cases with an overall prevalence of 50.52% of lipodystrophy cases. The prevalences of metabolic syndrome cases and lipodystrophy cases associated with the metabolic syndrome were 21.83% and 16.9% respectively. The management of these pathological entities (lipodystrophy and metabolic syndrome) has not yet been officially recognized in Cameroon and raises several problems affecting their diagnosis and treatment. The Ministry of Public Health should regularly provide equipments for the biological and medico-surgical management of the lipodystrophy; Facilitate the access of HIV-infected patients to lipid-lowering agents such as Pravastatin, Rosuvastatin and fibrates; Making more accessible the less toxic molecules such as FTC, ABC and TDF recommended in first-line treatment according to the new WHO recommendations as well as the proteases inhibitors considered to be less deleterious (Atazanavir, Saquinavir etc.) more accessible, and to appoint also in the care structures, the dieticians who will act as adviser for the HIV-infected patients about the respect of the standard hygiene-dietetic measures with regard to the lipodystrophy and metabolic syndrome. The scientific community should also carry out further investigations about the metabolic syndrome resulting from the abnormal distribution of fat in the body in order to know if all its components are known, such as the uricemia, which is an element totally ignored in all current definitions that have been the subject of an international consensus.

Authorship contribution

All authors contributed to the designing, preparation, editing, and final review of the manuscript.

Acknowledgements

Authors thank the collaborators of their respective institutions for the comments on the manuscript.

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