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Prevalência de Síndrome Metabólica em doentes VIH sob terapêutica antirretroviral

Prevalence of Metabolic Syndrome in HIV patients under highly active antiretroviral therapy

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/ Resumo

Introdução: O tratamento com terapêutica antirretroviral (TARV) reduziu a morbilidade e mortalidade associadas ao VIH. Com o aumento da esperança de vida, aumentou também a prevalência de obesidade, hipertensão arterial, dislipidemia e diabetes mellitus, fatores de risco cardiovascular que constituem a síndrome metabólica (SM). O objetivo deste estudo foi avaliar a prevalência do SM em pacientes VIH+ sob TARV.

Métodos: estudo transversal descritivo, entre julho e dezembro de 2014, incluindo 240 pacientes sob TARV ≥ 6 meses. SM foi definido de acordo com o National Cholesterol Education Program (NCEP 2001), a American Heart Association (AHA 2005) e a International Diabetes Federation (IDF 2006).

Resultados: De acordo com a definição da IDF, a prevalência de obesidade central foi 45.8%, hipertensão arterial 24.6%, hipertrigliceridemia 37.5%, baixo HDL 39.2% e intolerância à glicose 14.2%. A prevalência da SM de acordo com o NCEP, a AHA e a IDF foi 24.6%, 26.2% e 28.8%, respetivamente. Parece haver aumento da incidência com a idade, sexo feminino, baixo nível de instrução e tempo de TARV, particularmente com inibidores da protease.

Conclusão: O envelhecimento da população VIH+ e uso a longo prazo de TARV está a conduzir a uma maior prevalência de SM nesta população obrigando a uma maior reflexão na escolha de medicamentos antirretrovirais.

Palavras-chave: VIH; síndrome metabólica; risco cardiovascular

/ Abstract

***Introduction**: Treatment with antiretroviral therapy (ART) has reduced the morbidity and mortality associated with HIV. As the average life expectancy increases, obesity prevalence, hypertension, dyslipidemia and diabetes mellitus, which constitute cardiovascular risk factors for metabolic syndrome (MS) have also increased. The aim of this study was to evaluate the prevalence of metabolic syndrome in HIV patients under ART.*

***Methods**: A descriptive cross-sectional study between July and December 2014, including 240 patients on ART ≥ 6 months. MS was defined according to the National Cholesterol Education Program (NCEP 2001), American Heart Association (AHA 2005) and International Diabetes Federation (IDF 2006).*

***Results**: According to the IDF definition, the prevalence of central obesity was 45.8%, hypertension 24.6%, hypertriglyceridemia 37.5%, low HDL 39.2% and glucose intolerance 14.2%. The prevalence of MS according to the NCEP, AHA and IDF was 24.6%, 26.2% and 28.8%, respectively. There seems to be an increase in the incidence of MS with age, female gender, low level of education and time of ART, particularly with protease inhibitors.*

***Conclusion**: Aging of the HIV patients and long-term use of ART is leading to a higher prevalence of MS in this population forcing further consideration in the selection of antiretroviral drugs.*

***Key-words:** HIV; metabolic syndrome; cardiovascular risk*

/ Introduction

The introduction and widespread use of highly active antiretroviral therapy (HAART) has led to a substantial decline in the events related to immunodeficiency and mortality in HIV-infected individuals [1-3]. As a result, the average life expectancy has increased, leading to exposure to aging effects and environmental risk factors known to have an important impact in general population on the occurrence of obesity, diabetes mellitus (DM) and cardiovascular disease (CVD) [4-5].

Metabolic Syndrome (MS) includes a combination of risk factors that lead to CVD as the primary clinical outcome, such as obesity (especially central), changes in glucose metabolism (type II diabetes, impaired glucose tolerance or impaired fasting glycaemia), high blood pressure (HBP), hypertriglyceridemia and low HDL-c. The prevalence varies according to age, gender, ethnicity, and the definition used [6].

Within the general United States population, MS was estimated at 34.2% and this number has grown steadily over time [7]. In Europe the values are lower, with a recent British study in a cohort of middle-aged men to report prevalence of MS in 26% [8]. Finally, in Portugal, the first study on the prevalence of MS and its implications in cardiovascular risk - VALSIM Study [9] - showed that in adult users of primary health care the prevalence is high, reaching 27.5%. The increasing prevalence of MS is related to unbalanced food intake, physical inactivity and obesity, which peaked in the developed world.

There are various definitions of MS, which all share the same components but witch differ with regards to critical values for each component [10] – Table I.

In the new era of HAART, HIV patients are now exposed to changes in lipid metabolism leading to hypertriglyceridemia, hypercholesterolemia and other metabolic disorders, such as insulin resistance, hyperglycemia and redistribution of body fat with several studies showing high prevalence of MS in this population, with rates ranging from 11.4% to 43.2%, making HIV infection a high cardiovascular risk marker [14-18].

Since the description of lipodystrophy associated to therapy with protease inhibitors (PI) mainly the drug combination saquinavir/ritonavir [19], several other metabolic disorders have been studied in HIV individuals. The main alterations were dyslipidemia, insulin resistance and lipodystrophy, factors that are included in the MS criteria, generating a growing concern that the metabolic complications associated with HIV and HAART can lead to an increased risk of cardiovascular events. These metabolic changes may explain, at least partially, the fact that cardiovascular disease is now as important cause of morbidity/mortality in the HIV population as in the general population.

TABLE I - METABOLIC SYNDROME DEFINITIONS			
DEFINITION	**NCEP/ATP III (2001)[11]**	**AHA-NHLBI (2005) [12]**	**IDF (2006) [13]**
Mandatory criteria	None	None	Waist circumference# with ethnicity-specific values
Additional criteria	At least three of the following:	At least three of the following:	At least two of the following:
Central obesity	Waist circumference ≥ 102cm (male), ≥ 88cm (female)	Waist circumference ≥ 102cm (male), ≥ 88cm (female)	See mandatory criteria
Dyslipidemia	TG ≥ 150mg/dl OR HDL-C < 40mg/dL (male), < 50mg/dL (female)	TG ≥150mg/dl OR HDL-C <40mg/dL (male), <50mg/dL (female) OR treatment for this lipid abnormalities	TG ≥150mg/dl OR HDL-C <40mg/dL (male), <50mg/dL (female) OR treatment for this lipid abnormalities
Blood pressure	≥ 130/85mmHg	≥ 130/85mmHg OR treatment of previously diagnosed hypertension	Systolic BP >130mmHg OR diastolic BP >85mmHg, OR treatment of previously diagnosed hypertension
Glucose metabolism	Fasting plasma glucose ≥110mg/dl	Fasting plasma glucose ≥100mg/dL OR treatment of previously diagnosed DM	Fasting plasma glucose ≥100mg/dL OR treatment of previously diagnosed DM

If BMI >30kg/m2, central obesity can be assumed and waist does not need to be measured [in Europe, central obesity defined by waist circumference ≥ 94cm (male), ≥ 80cm (female)]. BP: Blood Pressure; TG: triglyceride; DM: Diabetes mellitus

/ General objective

This study aims to determine the prevalence of MS in HIV-infected patients under highly active antiretroviral therapy (HAART), followed in our outpatient clinic.

/ Methodology

Study design: cross-sectional study over a period of 6 months from July to December 2014.

Participants: HIV-infected patients managed at our outpatient clinic in Hospital de São José, Centro Hospitalar Lisboa Central, EPE - Lisboa

Inclusion criteria:

- HIV-1 or HIV-2 infection;
- age ≥ 18 years old;
- on combined antiretroviral therapy (HAART) for ≥ 6 months
- written given consent.

Exclusion criteria:

- withdrawal of HAART or duration of therapy inferior to 6 months

Sample dimension: During the considered time period there were 1014 appointments corresponding to 690 patients and of these 240 met the inclusion criteria.

Data collected:

- Anthropometric data: age, gender, weight, height, waist circumference and body mass index (BMI).
- Clinical data: immunological (TCD4+ cell) status at time of HAART initiation, current viral load and TCD4+ count and time in months of HAART. We assessed personal and family history of hypertension, dyslipidemia, diabetes mellitus, stroke or ischemic heart disease; smoking and drinking habits.
- Lab data: levels of fasting glucose in blood (and HbA1c, when appropriate), triglycerides, total cholesterol, LDL and HDL.

Definitions:

- Patients with BP values ≥135/85mmHg or under antihypertensive therapy were considered hypertensive. The stages of arterial hypertension were defined using the European Society of Cardiology (ESC) Guidelines published in 2013 (http://eurheartj.oxfordjournals.org/content/ehj/34/28/2159.full.pdf).
- Patients with fasting glucose ≥126mg/dl (2 measurements within 6 months), HbA1c≥6% or under oral antidiabetic were considered diabetic.
- Hypertriglyceridemia was defined as triglycerides ≥150mg/dl, hypercholesterolemia as total cholesterol ≥200mg/dl or LDL ≥100mg/dl and low-HDL as HDL <40mg/dl (women) or <50mg/dl (men).

- Metabolic syndrome (SM) was determined according to the definitions of the National Cholesterol Education Program/ Adult Treatment Panel III (NCEP/ATP-III 2001), the American Heart Association/National Heart, Lung, and Blood Institute (AHA/ NHLBI 2005) and the International Diabetes Federation (IDF 2006).
- HIV infection was defined using the CDC Revised Surveillance Case Definition for HIV Infection, 2014 (http://www.cdc.gov/hiv/statistics/recommendations/terms.html).

Student's t test and chi-square test were performed to assess differences between groups (numerical and categorical variables, respectively), using Excel 2010. A p-value < 0.05 was considered statistically significant.

/ Results

A total of 240 patients were included in this study, of which 166 (69.2%) were male and 74 (30.8%) were female. The average age was 47.4 years old. Approximately half of the patients (n=119; 49.6%) were smokers and 57 (23.8%) had a history of chronic alcohol consumption. About one third of the patients (n=75; 31.2%) only had primary school education and only 45 patients (18.8%) had been to college.

The majority of the patients (n=233; 97.1%) were infected with HIV-1, 6 patients (2.5%) were infected with HIV-2 and 1 patient (0.4%) was infected with both HIV 1+2. More than half of the patients (n=146; 60.8%) were asymptomatic at the time of the diagnosis (Stage A of the CDC HIV Classification, 2014) but with 44 patients (30.1%) showing severe immunodeficiency with TCD4+ count <200cells/mm^3. In contrast, and as expected, of the 80 patients who presented with symptoms suggestive of AIDS (Stage C), 62 (77.5%) showed TCD4+ counts in that order (<200cells/mm^3). The average TCD4+ count at the begging of HAART was 223.4 cells/mm^3.

In 199 patients (82.9%) the infection was acquired through sexual intercourse, primarily heterosexual route – 130 patients (54.2%), followed by homosexual intercourse – 69 patients (28.8%). Transmission of the virus by sharing needles associated with intravenous drug use was the third highest cause of infection – 31 patients (12.9%), and in a minority of the cases, other routes of transmission such as vertical transmission or blood transfusions were reported as being the cause of infection.

When family history of cardiovascular disease was considered regarding 1st degree relatives, 87 patients (36.2%) reported a family history of high blood pressure, 60 patients (25.0%) reported a family history of type II diabetes, 50 patients (20.8%) reported a family history of previous stroke and 41 patients (17.1%) reported a family history of ischemic heart disease.

Of the 240 patients included in the study, 59 (24.6%) were hypertensive - 34 (57.6%) with blood pressure levels classified as "Normal High" (systolic blood pressure (SBP) >130-139mmHg and/or diastolic blood pressure (DBP) >85-89mmHg), 24 patients (40.7%) "Stage 1 Hypertension" (SBP >140-159mmHg and/or DBP >90-99mmHg) and 1 patient (1.7%) "Stage 2 Hypertension" (SBP >160mmHg and/or DBP >100mmHg).

Of these 59 hypertensive patients, 45 were treated with antihypertensive drugs:
- angiotensin converting enzyme inhibitor (ACEIs) - 25 patients (55.6% of patients on antihypertensive therapy);
- calcium channel blockers (CCBs) - 19 patients (42.2%);
- diuretics - 9 patients (20.0%);
- angiotensin receptor blockers (ARBs) - 7 patients (15.6%);
- beta-blockers - 3 patients (6.7%);
- alpha-blockers, vasodilators and anti-angina drugs, each one with 1 patient.

More than half of this patients (n=27; 60.0%) were treated with just 1 antihypertension drug, 15 patients (33.3%) were on a combination of 2 drugs and 3 patients (6.7%) were on a combination of 3 drugs.

Lipid profile was evaluated according to mean values of total cholesterol (TC), LDL-C, HDL-C, triglycerides (TG): TC 186.5 mg/dl, LDL 125.9 mg/dl, HDL 47.4 mg/dL and TG 140.7 mg/dl. About one third of our patients (n=78; 32.5%) were on lipid-lowering therapy - 71 patients (29.6%) were doing statins, 13 patients (5.4%) were on fibrates, and ezetimib was being used by 2 patients (0.8%).

The diagnosis of type II diabetes was established in 23 patients (9.6%). Of these, 20 patients (87.0%) were on medication: 3 patients (15.0%) were doing insulin therapy and the other 17 patients (85.0%) were given oral antidiabetic drugs - biguanides (metformin) in 13 patients, DPP4 inhibitors (sitagliptin and vildagliptin) in 7 patients, sulfonylureas (glibenclamide and gliclazide) in 5 patients and acarbose and pioglitazones each in 1 patient.

With regards to the biometric characteristics we obtained an average body weight of 71.6Kg, average height of 1.71m and average body mass index of 26.1Kg/m2 (112 patients had BMI ≥ 25 kg/m2 and of these, 31 patients had BMI ≥30kg/m2) with average abdominal perimeter of 90cm.

The component conditions of MS (as per the IDF 2006 definition) in the 240 HIV-infected patients evaluated are displayed in Table II.

As explained in the methodology, patients on HAART for ≥6 months which were compliant and adherent to therapy and under clinical surveillance were included in this study (minimum 6, maximum 228 months; mean 86.4 months). With regards to the immunological status, patients had mean TCD4+ count of 609.4 cells/mm^3 (minimum 93, maximum 1979 cells/mm^3) and most of them had undetectable HIV viral load (n=220; 91.7%). HAART distribution is showed in Table III.

TABLE II - COMPONENT CONDITIONS OF THE MS OF THE 240 HIV-INFECTED PATIENTS

VARIABLES	VALUES N (%)
Waist circumference	
≥94cm in men	56 (23.3% total; 33.7% of men)
≥80cm in women	55 (22.9% total; 74.3% of women)
Blood pressure	
≥130/85mmHg	59 (24.6%)
HDL cholesterol	
<40mg/dl in men	63 (26.2% total; 38% of men)
<50mg/dl in women	31 (12.9% total; 41.9% of women)
Triglycerides	
≥150mg/dl	90 (37.5%)
Glucose	
≥110mg/dl	34 (14.2%)

Regarding HAART, 74 patients (30.8%) had regimens based on Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs), with the most used fixed dose combination being EFV/TDF/FTC (n=68; 28.3%), followed by RPV/TDF/FTC, also in a fixed dose combination, in 5 patients (2.1%); and EFV + ABC/3TC in 1 patient (0.4%). Around half of the patients (n=111; 46.3%) had regimens based on Protease Inhibitors (PI´s) with the most prescribed combination being DRV/r + TDF/FTC in 54 patients (22.4%), followed by ATV/r + TDF/FTC in 33 patients (13.8%), DRV/r + ABC/3TC in 17 patients (7.1%) and ATV/r + ABC/3TC in 7 patients (2.9%). Of the 240 patients included in the study, only 3 (1.2%) were treated with a regimen based on Integrase Inhibitors (II), in this case raltegravir and only 1 patient (0.4%) was treated with CCR5 Receptor Antagonist (maraviroc). A considerable amount of patients (n=52; 21.7%) were on alternative regimens, usually because of side effects, resistance mutations or pharmacological interactions.

The prevalence of MS in this study according to NCEP criteria/ ATP-III 2001, AHA/NHLBI 2005 and IDF 2006 was 24.6% (n=59), 26.2% (n=63) and 28.8% (n=69) respectively. The agreement between the different definitions was moderate and only 21.7% (n=52) of the individuals diagnosed by any of the definitions simultaneously met the criteria of all the others.

Amongst the 163 patients that did not have MS according to any of the previously mentioned definitions, 49 did not have any criterion, 62 had only one and 52 had two criteria. There were 25 patients who had MS according to the IDF 2006 definition but not according to the other two definitions. Of the 52 patients that met all MS definitions, only 3 met the five criteria. The demographic details of the patients with and without MS are showned in Table IV.

TABLE III – HAART DISTRIBUTION
(based on EACS 7.1 guidelines http://www.eacsociety.org/files/guidelines-7.1-english.pdf)

NNRTI´s based regimens – n = 74	
EFV/TDF/FTC (co-formulated)	68 (28.3%)
RPV/TDF/FTC (co-formulated)	5 (2.1%)
EFV + ABC/3TC	1 (0.4%)
II´s based regimens – n = 3	
RAL + TDF/FTC	3 (1.2%)
PI´s based regimens – n = 111	
DRV/r + TDF/FTC	54 (22.5%)
ATV/r + TDF/FTC	33 (13.8%)
DRV/r + ABC/3TC	17 (7.1%)
ATV/r + ABC/3TC	7 (2.9%)
Others – n = 52	
NVP+TDF/FTC	9 (3.8%)
NVP+ABC/3TC	4 (1.7%)
EFV+ABC+TDF	1 (0.4%)
EFV+ZDV/3TC	1 (0.4%)
LPV/r + TDF/FTC	8 (3.3%)
DRV/r + ABC + TDF	3 (1.2%)
LPV/r + ABC/3TC	3 (1.2%)
ATV/r + ABC/3TC + TDF	3 (1.2%)
DRV/r + ABC/3TC + TDF	3 (1.2%)
FPV/r + TDF/FTC	2 (0.8%)
DRV/r + ddI + TDF	1 (0.4%)
DRV/r + TDF + ETV	1 (0.4%)
ATV/r + ABC + TDF	1 (0.4%)
ATV/r + ddI + FTC	1 (0.4%)
ATV/r + TDF + ZDV/3TC	1 (0.4%)
LPV/r + ABC/3TC + TDF	1 (0.4%)
LPV/r + ZDV/3TC	1 (0.4%)
RAL + LPV/r	3 (1.2%)
RAL + DRV/r	2 (0.8%)
RAL + DRV/r + TDF	1 (0.4%)
RAL + ETV	1 (0.4%)
MVC + TDF/FTC + DRV/r	1 (0.4%)

LEGENDA: 3TC lamivudine; **ABC** abacavir; **ATV/r** ritonavir-boosted atazanavir; **ddI** didanosine; **DRV/r** ritonavir-boosted darunavir; **EFV** efavirenz; **ETV** etravirine; **FTC** emtricitabine; **FPV/r** ritonavir-boosted fosamprenavir; **II** integrase inhibitor; **LPV/r** ritonavir-boosted lopinavir; **MVC** maraviroc; **NVP** nevirapine; **NRTI** nucleoside reverse transcriptase inhibitor; **PI** protease inhibitor; **RAL** raltegravir; **RPV** rilpivirine; **TDF** tenofovir disoproxil; **DV** zidovudina

/ Discussion

Using the three definitions, we obtained MS prevalence rates between 24.6% and 28.8%, which closely overlap the values found in VALSIM Study for the uninfected Portuguese population [9].

As found in other studies, analysis of the 52 patients diagnosed with MS according to all three definitions showed that prevalence of MS appears to increase with age [7.7% <35 years old (yo);

TABLE IV - DEMOGRAPHIC DETAILS OF THE PATIENTS WITH AND WITHOUT METABOLIC SYNDROME (SM)

CHARACTERISTIC	MS (BY THE THREE DEFINITIONS)	NO MS	P-VALUE
n (%)	52 (21.7%)	188 (78.3%)	-
Male (n/%) Female (n/%)	30/57.7% 22/42.3%	136/72.3% 52/27.7%	0.021
Age (years; mean)	55.9	45.1	<0.0001
Level of education (n/%)			
- ≤4ºgrade	54/40.4%	21/28.7%	<0.0001
- ≤7ºgrade	20/15.4%	8/10.6%	0.003
- ≤9ºgrade	37/11.5%	6/19.7%	0.171
- ≤12ºgrade	40/17.3%	9/21.3%	0.558
- Graduate	37/15.4%	8/19.7%	0.452
Smoking (n/%)	16/30.8%	103/54.8%	0.002
Alcoholism (n/%)	11/21.1%	46/24.5%	0.310
Family history (n/%)			
- High blood pressure	19/36.5%	68/36.2%	0.961
- Type II diabetes	12/23.1%	48/25.5%	0.359
- Myocardia infarct	12/23.1%	29/15.4%	0.196
- Stroke	14/26.9%	36/19.1%	0.223
High blood pressure (n/%)	34/65.4%	25/13.3%	<0.0001
Type II diabetes (n/%)	16/30.8%%	7/3.7%	<0.0001
BMI (Kg/m2; mean)	30.7	24.1	0.026
Waist (cm; mean)	101.0	86.9	<0.0001
Total cholesterol (mg/dl; mean)	193.1	184.7	0.179
HDL (mg/dl ; mean)	41.7	49.1	0.042
LDL (mg/dl; mean)	132.0	124.2	0.037
TG (mg/dl; mean)	200.0	124.3	0.003
Nadir CD4+ (cells/mm^3; mean)	212.8	226.3	0.297
Current drug therapies (n/%)			
- NRTI	49/94.2%	185/98.4%	0.088
- NNRTI	11/21.1%	79/42.0%	0.005
- PI	41/78.8%	106/56.4%	0.003
- II	5/9.6%	5/2.7%	0.026
- CCR5 antagonist	1/1.9%	-	-
Current CD4+ (cells/mm^3; mean)	592	614.2	0.309
Undetectable HIV viral load (n/%)	49/94.2%	171/91.0%	0.451
HAART duration (months; mean)	94.7	84.1	0.117

12.8% 35-50 yo; 39.8% >50 yo; p-value <0.0001], as well as with low level of instruction (with MS: 21/41.4% ≤4ªdegree; without MS: 54/28.7% - p-value < 0.0001), high BMI (30.7 with MS vs 24.1 without MS - p-value 0.026) and also showed higher expression in females (p-value 0.021) – although women made up for only 30.8 % (n=74) of the general population involved in this study, they were responsible for almost half the cases of MS found - 42.3 % (n=22).

Comparing the route of transmission between the group with MS and the group without it, in the first one we have a higher percentage of infection acquired through heterosexual intercourse (73.1% with MS vs 48.9% without MS) as opposed to other routes of transmission, like homosexual intercourse (15.4% with MS vs 32.5% without MS) or intravenous drug use (7.7% with MS vs 14.4% without MS). These differences can probably be explained because of a higher percentage of women in the group with MS.

When comparing the route of transmission in both groups of men (with MS and without MS) it was found that in the first group (men with MS) heterosexual intercourse was the main cause of infection - 60.0% with MS vs 33.8% without MS, as opposed to the second group (men without MS) where homosexual intercourse was the main cause of HIV infection - 26.6% with MS vs 44.1% without MS. These variances are expected when the average age of men in both groups is so different – 54.9 years old with MS vs 45.4 years old without MS.

Contrary to expectations, smoking and alcohol consumption, known as cardiovascular risk factors particularly due to an increase in high blood pressure and dyslipidemia, were not more prevalent in this group as opposed to the rest of the patients. This could be a result of our multidisciplinary team effort towards increasing awareness on the importance of diet control, tobacco and alcohol consumption.

There seems to be a relationship between the CD4+ nadir and the presence of MS – 212.8 cells/mm^3 (with MS) and 226.3 cells/mm^3 (without MS), as showed by Jericó et al [20] in a cohort of 710 HIV-infected patients, although it was not statistically significant (p-value 0.297).

The average duration of ART in those with MS according to all the definitions was 97.4 months, higher than the average of the population in the study (86.4) but also with a non-significant p-value (0.117). More than ¾ (n=41; 78.8%) of the patients with MS were treated with regimens containing protease inhibitors, as opposed to the group without MS where PI were used only in half of the cases (p-value 0.003) – consistent with the study by Samaras K et al [15] where a significantly higher prevalence of MS in patients under protease inhibitors is reported (p-value 0.004).

About ¼ of the patients (n=52; 21.7%) were on alternative regimens, usually because of side effects, resistance mutations or pharmacological interactions – the concept of polypharmacy is now a reality in HIV patients leading to drug interactions, particularly associated with proton pump inhibitors or lipid lowering drugs, sometimes forcing to HAART changes.

Even though MS amongst HIV patients is a reality known worldwide, as well as the association with protease inhibitors, we still witness high prevalence of regimens containing PI´s, not only at Hospital de São José but also in the rest of the country – data from the Portuguese report "Portugal - Infecção VIH, SIDA e Tuberculose em números – 2014" [21] demonstrates that at the end of 2013, almost half of the patients (n=12.634.164; 44.8%) were under therapy with protease inhibitors. Also, and in parallel with the results of our study, this report ratifies the low prevalence of regimens containing integrase inhibitors, with just 5.5% of the Portuguese HIV population under HAART doing Raltegravir, the only II available at the time. No recent data is available.

This could be partially explain by the Portuguese HIV most recent guidelines – "Recomendações Portuguesas para o tratamento da infeção por VIH-1 e VIH- 2, 2015 Versão 1.0" [22] that consider Raltegravir an alternative only when there are important drug interactions as opposed to, for example, the latest Spanish Gesida Guidelines (2015) [23] where the integrase inhibitors based regimens are preferred compared to the ones containing NNRTI´s or PI´s.

Also, comparison of the cost of TDF/FTC+RAL and ABC/3TC+RAL in our Hospital (unpublished data) with other regimens containing PI´s or NNRTI´s suggests it would be more expensive to initiate antiretroviral treatment with II´s even though we are just comparing the price of the drug and not the other costs including those incurred while managing adverse effects or the costs of drug-resistance studies. A cost-efficacy analysis should be executed in order to maximize the population's health outcomes in a context of inherently limited resources.

Table V compares the prevalence of the defining criteria of MS, according to the definition by NCEP/ATP III 2001, in our study group and in the VALSIM study. Although most of these percentages are higher in the patients of the VALSIM study, this is probably due to a difference in the average age of the population included: HIV 47.4 years of age Vs non-HIV 58.1 years of age. However, it is evident the dominance of HIV infected patients with respect to changes in the lipid metabolism, associated with natural progression of HIV infection, the HIV virus himself and therapy – the same findings were describe by Bernal E et al in patients with HIV infection from a Mediterranean cohort [14].

TABLE V - COMPARISON OF MS CRITERIA IN HIV PATIENTS VS NON HIV

MS CRITERIA	HIV	NON HIV
Glucose intolerance	14.2%	18.5%
Central obesity	27.9%	46.3%
Hypertension	24.6%	56.9%
Low HDL cholesterol	39.2%	25.0%
Hypertriglyceridemia	37.5%	30.7%

The general population there has shown an increase of epidemic proportions in the prevalence of obesity, insulin resistance, hypertension and associated complications. The results of our study suggest that HIV individuals on HAART do not appear to be spared of this epidemic, as shown by the high rates of obesity, hyperglycemia, hypertension and dyslipidemia.

Limitations of the present study are mainly related to the fact that the measurements perhaps were not conducted in a uniform manner including waist circumference and blood pressure and also that other variables should have been taken into consideration such as physical activity, diet, clinical manifestations of lipodystrophy and DEXA (dual energy X-ray absorptiometry) scan results.

/ Conclusion

HAART obvious benefits exceed the potential cardiovascular risk associated to antiretrovirals, but it should be taken into account that general population risk factors now overlap with specific ones in this population like the premature aging associated with HIV infection and adverse long-term effects of antiretrovirals. Quickness on identifying Metabolic Syndrome seems to be a useful tool to recognize HIV patients at higher risk and define therapeutic strategies in order to reduce cardiovascular diseases and diabetes burden in this population.

/ Declaration of interest

The authors declare that there are no conflicts of interest in relation to this article

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