ORIGINAL RESEARCH PAPER

Cardiology

DYSLIPIDEMIA IN PATIENTS LIVING WITH HIV IN DAKAR ; CASE-CONTROL, CROSS-SECTIONAL, MULTICENTRIC STUDY

KEY WORDS: HIV, antiretrovirals, dyslipidemia, cardiovascular risk, Senegal

Mingou JS*	Department of Cardiology University Hospital Aristide Le Dantec, Dakar SENEGAL *Corresponding Author
Aw F	Department of Cardiology University Hospital Aristide Le Dantec, Dakar SENEGAL
Sarr SA	Department of Cardiology University Hospital Aristide Le Dantec, Dakar SENEGAL
Ngaide AA	Department of Cardiology University Hospital HOGGY, Dakar SENEGAL
Dioum M	Department of Cardiology FANN University Hospital Center, Dakar SENEGAL
Coly S	Department of Cardiology University Hospital Aristide Le Dantec, Dakar SENEGAL
Bodian M	Department of Cardiology University Hospital Aristide Le Dantec, Dakar SENEGAL
Ndiaye MB	Department of Cardiology University Hospital Aristide Le Dantec, Dakar SENEGAL
Mbaye A	Department of Cardiology University Hospital HOGGY, Dakar SENEGAL
Kane Ad	Department of Cardiology Saint Louis Regional Hospital Regional, Saint Louis SENEGAL
Ly F	Department of Dermatology Institute of Social Hygiene, Dakar SENEGAL
Diao M	Department of Cardiology University Hospital Aristide Le Dantec, Dakar SENEGAL
Ndour CT	Department of Infectious Diseases FANN University Hospital Center, Dakar SENEGAL
Kane A	Department of Cardiology University Hospital HOGGY, Dakar SENEGAL
Ba SA	Department of Cardiology University Hospital Aristide Le Dantec, Dakar SENEGAL

ABSTRACT

HIV infection is a cardiovascular risk factor. With antiretroviral triple therapy, patients life expectancy is increasing, but the induction of metabolic, dyslipidic, insulin resistance, and clinical lipoatrophy are leading to earlier coronary or cerebrovascular complications. We wanted to study the prevalence and lipid profile of people living with HIV (PLWHIV) in a multicenter case-control study conducted in different hospitals in Dakar (Senegal). From this serie, we observed a statistically more frequent total hypercholesterolemia (p = 0.001) in treated PLWHIV, a statistically more frequent hypoHDLemia in untreated PLWHIV (p = 0.03), and a higher cardiovascular risk in PLWHIV on anti-retroviral therapy (ARV) (p = 0.01).

Introduction

The increasing effectiveness of ARV (antiretroviral) therapy for people with HIV has significantly improved the patients life expectancy. However, there is a question about the effects of the disorders related to this treatment. These include metabolic syndrome, diabetes mellitus and dyslipidemia. These dreaded lipid disorders, because of their atherogenic potential widely described in developed countries, are paradoxically sparsely studied in Sub-Saharan Africa where live the vast majority of people infected with HIV.The overall objective of this work was to assess the prevalence of dyslipidemia in HIV patients on treatment compared to those without treatment and compared to naive patients. The next step was to assess the cardiovascular risk and to compare it with the different groups.

Patients and Methods

Our study was carried out in Dakar at the cardiology clinic, in the dermatology department of Aristide Le Dantec University Hospital and King Baudouin Hospital of Guediawaye. This is a multicenter study conducted over a 10-month period from January 2011 to October 2011.

The inclusion criteria were as follows:

- Be at least 18 years old regardless of gender
- Being infected with HIV / AIDS and being on ARV: 1st group
- Being infected with HIV / AIDS and not treated with ARV: 2nd group

The first two groups consisted of subjects regularly followed in the dermatology department of the University Hospital Aristide Le Dantec and the King Baudouin Hospital.

The control group (free from HIV / AIDS) was constituted after a retroviral serological test by rapid diagnostic method.

In addition to the agreement of the various heads of structures, we had gathered in each patient a free and informed consent. All patients had benefited from free clinical and paraclinical examinations.

Preventive and therapeutic advice was offered to any patient with risk factors and / or cardiovascular events.

Were not included non-consenting HIV positive patients, patients with another cause of clinically detectable dyslipidemia, patients hospitalized with AIDS, patients on contraception or who were pregnant.

The questionnaire collected socio-demographic data, cardiovascular risk factors and retroviral status.

A complete physical examination was done, but focused on the cardiovascular system, the respiratory system and the cutaneo-phanumerian system looking for complications.

On PLWHIV, we determined the clinical stage, based on the 1993

CDC classification and definition of AIDS [1].

In biology, blood samples were taken after 12 hours of fasting on two tubes, a dry tube and an EDTA tube. For the blood samples on dry tubes, the sera were decanted after centrifugation at 2000 rpm for 5 minutes and aliquoted in two cryotubes, one cryotube for the determination of the serology and the other for the determination of lipids. The sera were preserved at -20 ° C until dosing. Lipid parameters were assayed with Biomérieux reagent kits with enzymatic methods coupled with colorimetry. In our study, the results were validated by the determination of accuracy and precision by daily quality control, from a normal control serum and a pathological control serum introduced into the dosing series.

Dyslipidemia has been defined for total cholesterolemia greater than 2g/l and/or LDL cholesterol higher than 1.3 g / l or associated risk factors and/or HDL cholesterol lower than 0.35 g / l and / or triglyceride levels greater than 1.5 g / l according to the recommendations of NCEPIII [2].

Retroviral serology was performed with a mixed screening test and a discriminatory HIV-1 and HIV-2 screening test, based on the HIV testing strategy in Senegal [3]. The mixed screening test was conducted using the ELISA technique with the Genscreen Plus HIV Ag-Ab reagent kit (Biorad) and the discriminatory screening test using a rapid test with the ImmunoComb II HIV 1 & 2 BiSpot (PBS Orgenics) reagent kit. The analytical methods used to determine HIV serology have been validated at the laboratory by determining sensitivity, specificity, positive and negative predictive values. A count of CD4 lymphocytes by flow cytometry was made. The viral load was quantified by the Roche Amplicor HIV method with a lower detection limit of 50 copies/ml.

A 12-lead resting electrocardiogram that revealed signs of cavitary hypertrophy, disturbances in pace and conduction, and signs of myocardial necrosis.

A transthoracic Doppler echocardiography that appreciated the cardiac dimensions for hypertrophy and / or left ventricular dilation, to evaluate the kinetics of the left ventricular walls, the existence of intra-cavitary thrombi. The Doppler study evaluated the diastolic function of the left ventricle and pulmonary arterial pressure.

The results were entered and analyzed using EPI Info software version 3.3.2.

The descriptive study was done by calculating or determining position parameters (frequency for categorical variables and average, median and mode for quantitative variables) and dispersion parameters (standard deviation, IQR: interquartile range).

The analytical study was done with the crossed tables. To compare the proportions we used the Chi square test (Pearson and Yates) and the Chi square test for trend (if one of the variables was ordinal), with an alpha significance threshold of less than 0.05. The odds ratio surrounded by its confidence interval made it possible to quantify the strength of the association.

Results:

Our study involved 186 individuals whose distribution is shown in Figure 1.

The average age of the subjects was 42.4 years. There was a predominance of women who accounted for 75.8% of the population (n = 141) with a sex ratio of 0.31.

Among PLWHIV, 91.5% were HIV-1 infected, 5% HIV-2 and 3.5% had HIV-1 and HIV-2.The average CD4 count was 477/mm^3 with extremes of 50 and 1743/mm^3 and a median of 413/mm^3. This rate was 440.33/mm^3 in treated HIV-positive patients versus 451.966/mm^3 in untreated ones.

The median duration of antiretroviral therapy was 45 months (range 2 to 96 months). Out of the treated patients, 43.7% had been under ART for more than four years.

Antiretroviral therapy used at first line 2 nucleoside reverse transcriptase inhibitor (NRTI) and 1 non-nucleoside reverse transcriptase inhibitor (NNRTI) in 83.2% of cases and at the second line in 16.8% 2NRTI and 1 protease inhibitor (PI). In patients on protease inhibitors, the average duration of treatment was 52 months with a median at 56 months (IQR: 31, 72).

The most common treatment regimen in the first line was Combivir + Nevirapine (43%), followed by Combivir + Efavirenz (26%).

Cardiovascular risk factors such as smoking, estrogen-progestative contraception, sedentary lifestyle, and systolic hypertension were significantly more found in treated or untreated HIV patients compared to controls as shown in Table 1.

However, diabetes, women's abdominal obesity and menopause were more frequent in controls compared to infected patients with no statistically significant link.

Regarding the lipid profile, dyslipidemia was uncommon in WHO Stage I and Stage 3 patients (10.7%) compared to WHO Stage 2 (64.3%). It was more common in HIV1-infected subjects (70.2%) than those infected with HIV2 (5.1%) and double-profile (1.3%).

The frequency of dyslipidemia was higher in subjects who had a CD4 count of less than 200 (n = 14) or 61%, compared to those who had a CD4 greater than 200 (n = 42) or 45% (p = 0.5).

The prevalence of hypercholesterolemia was statistically more significant (p = 10-3) in treated PLWHIV compared to other groups. The prevalence of hypocholesterolemia was more significant among untreated PLHIV compared to the others (Table 2).

The prevalence of dyslipidemia was higher in individuals who were on the second-line protocol (2INTI + 1PI) (n = 8 or 66.7%) than in those who were on the first line protocol (2NRTI + 1NNRTI) (n = 32 or 41.6%) without a statistically significant link (p = 0.1).

Dyslipidemia was higher in patients receiving protease inhibitors (PI) except hyperLDLemia, which was not found in any patient under PI.

Total cholesterol was high in 21.5% of patients on PI versus 18.5% of patients who were not on PI.

HypoHDLemia was noted in 35.7% of patients on PI versus 22.6% of non-PI patients.

Hypertriglyceridemia was observed in 21.5% of patients on PI versus 18.6% of non-PI patients. Table 3 compares the results according to the therapeutic protocol used.

The frequency of dyslipidemia was higher in subjects who were on AZT, 3TC and nevirapine (38%) followed by those on AZT, 3TC and Efavirenz (31%). There was no statistically significant relationship (p = 0.3).

Discussion

The prevalence of HIV infection in Senegal is 0.7% with a female predominance (sex ratio between men and women = 2.25) [3]. Sawadogo [4] and Co. in Burkina had found this female predominance among PLWHIV.

Data from the literature in Europe, particularly with the DAD study (The data collection on adverse events on anti-HIV drug) [5] evaluating the prevalence of risk factors in HIV-infected individuals and Bergensen and Co [6] found a male predominance.

This predominance of the female gender in African studies could be explained by the vulnerability of women compared to men. It

should also be noted that our study was conducted in one of the mother-child pilot transmission centers, the King Baudouin Hospital.

The male predominance in Europe is linked to the high prevalence of homosexuality and drug addiction.

The cardiovascular risk for HIV-infected patients treated with antiretrovirals is higher than for untreated infected patients and the general population [7].

Our results corroborate this fact with, in particular, a higher cardiovascular risk for patients undergoing treatment versus those without ART (p = 0.01).

We also noted that the association of several risk factors (≥3 factors) was significantly more common among PLVIH, compared to controls (p = 0.03). In our series, 85% of treated HIV patients had more than two cardiovascular risk factors whereas, in the literature, only 30% of uninfected patients who had an acute coronary syndrome presented more than 2 cardiovascular risk factors [8].

All these findings point to a higher cardiovascular risk in patients treated with antiretrovirals when compared to untreated patients, but also, to HIV-negative patients according to most studies [5, 6, 9, 10, 11].

It is important to differentiate between the specific effect of HIV infection on plasma lipids and the effect of highly active antiretroviral therapy, the tritherapies that most often involve a nucleoside inhibitor (NRTI) or non reverse transcriptase (NNRTI), as well as a protease inhibitor (PI).

The occurrence of dyslipidemia has been known for a long time in patients with HIV infection. Our series report 61% (n = 14) of dyslipidemia in patients who had CD4 ratio<200 versus 45% (n = 42) of dyslipidemia in those with CD4 ratio > 200 (p = 0.5). A low level of CD4 and a high level of viral RNA are associated with low HDL levels in several studies [12; 13].

A total cholesterol level of 2.8% was observed in untreated PLHIV and 2% in controls. SAWADOGO and Co [4] in Burkina Faso also reported an increase in total cholesterol on infected patients. These results are contrary to most data in the literature [12; 13],who reports a decrease in total cholesterol in infected patients. In fact, total hypocholesterolemia appears very early in HIV-infected individuals, according to some authors, and is thought to be directly related to HIV infection and not to nutritional status alone [12; 13; 14].

Levels of LDL greater than 1.6 g / l were 4.3% in PLHIV treated versus 2.8% in untreated ones. These findings were also noted in the Sawadogo and Co study [4].

Low HDL-c levels were significantly higher in PLWHIV than in controls (p = 0.03).This decrease in HDL-c in infected patients has been reported by Ducobu and Co [15] in Belgium. Different mechanisms have been mentioned: HIV contributes to the decrease of HDL-c on one hand by altering the efflux of cholesterol from macrophages via the transporter ABCA1 [13], on the other hand by increasing the activity of certain enzymes such as hepatic lipase and phospholipase A2. [13]

HIV infection is associated to a change in the metabolism of HDL-c: cholesterol is redirected to Apo-B-rich lipoproteins and the reverse transport function of cholesterol is reduced. [16]

Triglyceride elevation was found in 6.2% of untreated PLHIV and in 14.6% of treated patients but non-statistically significant (p = 0.2), with an average value in infected patients which was twice that of control persons. This increase in triglycerides has been noted in several data from the literature [13,16]. These disturbances of triglyceride levels in HIV-infected individuals would be related to the effect of the various cytokines and tumor necrosis factor alpha. Interferon (INF) and TNF are correlated with hypertriglyceridemia [16].

The prevalence and degree of lipid abnormalities vary by molecule, within a single class, and possibly by duration of treatment [17,18]. According to Boccara [17], within the same class of ARV, there is a different impact of the various molecules on the lipid balance. In addition, some associations are more "lipidogenic" than others [19].

Indeed, it seems clear that the causes of lipid disorders in HIV-infected patients treated with ARVs are multiple and not exclusive of each other. They are pharmacological, viro-immune, nutritional, all reinforced by genetic predispositions [20].

Since the advent of triple therapy and the introduction of PIs, dyslipidemias have been observed under treatment. It has been shown that their frequency increases with the duration of ARV treatment : more than 50% of patients on PI after 2 years of treatment [21].

Our study found statistically more significant hyperchol esterolemia in treated PLWHIV compared to other groups (p = 0.001).

In a study comparing several combinations of ARV [22; 23; 24], first-line subjects treated with PI combinations had higher lipid levels and CT / HDL-c than controls. This finding was made in our series with a high index of atherogenicity in 11.2% (n = 10) of treated HIV patients, 9.1% (n = 3) of untreated HIV patients and 2% (n = 1) of controls.

In the APROCO cohort [22], which included 223 HIV-infected men and women under PIs versus 527 non-HIV male subjects, HIV-infected patients had low HDL-c levels and increased triglycerides.

In the study by Rhew and Co [25], two years after initiation of antiprotease treatment, 50% of patients had a total cholesterol greater than 2.3 g / l. These results are comparable to ours with an average duration of PI treatment of 52 months and 21.5% of patients with a high total cholesterol level. Another study conducted by Haugaard and Co. [21] showed that the use in naďve subjects of a treatment with an antiprotease compared to a treatment with 3 NRTIs induced a more marked increase of the cholesterolemia (+0,53 versus +0,09 µmol) with a larger number of patients with hypercholesterolemia.

This work reports more frequent dyslipidemia in subjects who were on NRTIs and PIs (66%) compared to those who were on NRTIs and NNRTIs with no statistically significant link.

Boccara [17] concluded that the NRTI and PI combination, after a few months of treatment, resulted in more metabolic abnormalities with lipodystrophic syndromes and glucose-lipid abnormalities. The combination of NRTIs with PIs, according to Capeau [18], would contribute, by mitochondrial toxicity, to accentuating the lipid and glycemic metabolic disorders of PIs. Elsewhere, various studies have shown an association between PI use and dyslipidemia [22; 6; 25].

In total,in our study, the majority of patients infected with HIV under anti-retroviral therapy, had an abnormal lipid profile with a high potential for cardiovascular disease in the near future.

Conclusion

Dyslipidemia is a major risk factor that is very common among PLWHIV. In addition, those treated with ARVs have a higher cardiovascular risk.

Conflicts of interest: None

Limits

One of the limitations of this study is the relatively small number of patients surveyed; we were faced with the refusal of some patients and especially controls (realization of HIV serology). It has been

difficult for us to recruit untreated HIV patients because, in our sites of recruitment, these patients most often came to a stage where they were already eligible for antiretroviral treatment. These constraints were a major obstacle for the match of controls with patients by age and sex, also posing a problem of comparability of our three study populations.

There was a bias related to the selection of our study population consisting of a relatively young cohort, followed since 2004 and, secondly, a bias related to the treatment regimen of our patients who were essentially in the front line. However, the second-line therapeutic protocol, composed of protease inhibitors, is better known in the genesis of metabolic disorders.

Because of these limitations and inherent biases in cross-sectional studies, the results presented should be considered as associations from which no conclusions about causality can or should be made. Therefore, additional cohort studies, or to a lesser extent, case-control studies are needed to confirm the differences between ARV-treated patients and the other two groups.

LIST OF FIGURES AND TABLES

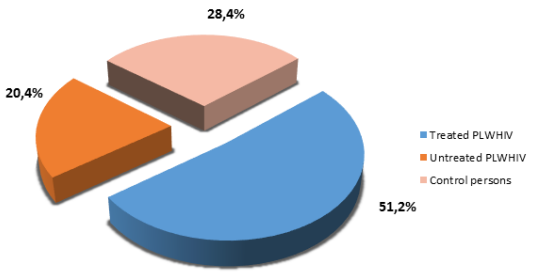

Figure 1 : Repartition of 186 patients according to different groups of comparison

Table1: Prevalence of different risk factors

Cardiovascular risk factors	Treated PLWHIV %	Untreated PLWHIV %	Control persons %	p-value
Age≥ 65 years (W) ≥ 50 years (M)	5, 3 41,7	0 12,5	5,7 25	0,3 0,5
Vascular heredity	4		2	
Tobacco	17	8	4	0,000
Abdominal obesity (M) (W)	2,2 34,9	0 18,6	0 46,5	0,4 0,0007
Physical inactivity	91,6	94,7	71,7	0,0008
Hypertension SBP≥140 DBP≥90	23,2 14,7	10,5 10,5	17,6 11,8	0,03 0,7
Diabetes	4,2	5,2	5,7	0,5
Atherogenic indice	11,2	9,1	2	0,15
Menopause	32	14,7	40,5	0,05
Hormonal contraception	1,6	20,6	6,5	0,01
Electric left ventricle hypertrophy	25,3	7,9	11,5	0,02
Cardiovascular risk factors≥3	32	7	12	0,03
Mean Framingham risk score	4.07	2.29	3,58	0.010

SBP : systolic blood pressure, DBP : diastolic blood pressure, W : women, M : men

Table2: Prevalence of dyslipidemia in our population

Dyslipidemias	Treated PLWHIV (n) %	Untreated PLWHIV (n) %	Control persons (n) %	p-value
History of dislipidemia	(4) 3,8	(0) 0	(3) 5,3	0,4
HDL< 0,4 g/l	(20) 23,2	(15) 42,1	(14) 24,5	0,03
LDL> 1,6 g/l	(4) 4,3	(1) 2,8	(0) 0	0,3
Triglycerides > 1,5 g/l	(13) 14,6 (19) 20,7	(2) 6,2 (1) 2,8	(3) 6,9	0,2 0,001
Total cholesterol > 2 g/l			(1) 2	

Table3:Repartition of dyslipidemias according to antiretroviral therapy protocole

Parameters of dyslipidemia	2NRTI+1NNRTI	2NRTI+1PI	P value
LDL-c>1,6 g/l	(3) 4%	(0) 0%	0,09
HDL-c<40 g/l	(17) 22,6%	(4) 35,7%	0,08
Total cholesterol> 2g/l	(14) 18,6%	(3) 21,5%	0,13
Triglycerides>1,5g/l	(11)17,4%	(2) 21,5%	0,5

NRTI : nucleoside reverse transcriptase inhibitors;NNRTI : non-nucleoside reverse transcriptase inhibitors; PI : protease inhibitors

REFERENCES

1. Barré-Sinoussi F. Virologie fondamentale de l'infection ŕ VIH. In: Girard PM, Katlama C, Pialoux G. VIH, edition 2007. Paris, DoinEditeurs 2007: 3-68
2. National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. Circulation. 2002; 106:3143–3421.
3. N M Manga, S A Diop, C T Ndour et al .Dépistage tardif de l'infection ŕ VIH ŕ la clinique des maladies infectieuses de Fann, Dakar : circonstances de diagnostic, itinéraire thérapeutique des patients et facteurs déterminants. Medmal.2009. 39 (2). 95-100
4. M Sawadogo, J Sakandé, E Kabré et al. Laboratoire de biochimie, CHU Yalgado Ouédraogo, Ouagadougou, Burkina Faso. Profil lipidique au cours de l'infection par le VIH ŕ Ouagadougou - Burkina Faso : intéręt des marqueurs lipidiques dans le suivi de l'évolution de l'infection ŕ VIH.Annales de Biologie Clinique.2005 ; 63(5) : 507-12p
5. Friis-Mřller N, Weber R, Reiss P, et al. DAD study group. Cardiovascular disease risk factors in HIV patients-association with antiretroviral therapy. Results from the DAD study. AIDS 2003;17 (8): 1179-93.
6. Bergersen BM, Sandvik L, Bruun J N et al. Elevated Framingham risk score in HIV-positive patients on highly active antiretroviral therapy: results from a Norwegian study of 721 subjects. Eur J Clin Microbiol Infect Dis., 2004 ; 23: 625-630.
7. Boccara F, Ederhy S, Janower S et al. Risque cardio-vasculaire chez le patient infecté par le VIH. MT Cardio., 2005 ; 1(2) : 195-200.
8. Grenier O, Cambou JP, Ferrieres J, et al. Baseline characteristics and management of patients less than 45 years of age hospitalized for acute coronary syndromes: results from the nationwide French PREVENIR 1 and PREVENIR 2 studies. Ann CardiolAngeiol, 2002; 51 : 15-19.
9. Savčs M, Chęne G, Ducimetičre P, et al. Risk factors for coronary heart disease in patients treated for human immunodeficiency virus infection compared with the general population. Clinical Infectious Diseases., 2003 ; 37: 292-298.
10. Kaplan RC, Kingsley LA, Sharrett AR et al. Ten-year predicted coronary heart disease risk in HIV-infected men and women. Clin Infect Dis., 2007; 45 (8): 1074–1081.
11. Loire R, Capron L. Vascular complications of HIV infection. STV 1995; 7 (7): 489-492.
12. El-Sadr W.M., C.M. Mullin, A. Carr et al. Effects of HIV disease on lipid, glucose andinsulin levels : results from a large antiretroviral naďve cohort. HIV Med 2005, 6 (2) : 114-121.
13. MujawarZ., H. Rose, M.P. Morrow et al. Human immunodeficiency virus impairs reverse cholesterol transport from macrophages. PLoSBiol2006, 4 (11): 365.
14. Grunfeld C, Pang M, Doerrler W et al. Lipids, lipoproteins, triglyceride clearance, and cytokines in human immunodeficiency virus infection and the acquired immunodeficiency syndrome. J Clin EndocrinolMetab 1992; 74 (5): 1045–52.
15. Ducobu J, Payen MC. Lipides et sida. Rev Med Brux 2000; 21(1): 11-7.
16. Haugaard SB, Andersen O, Pedersen SB et al. Tumor necrosis factor alpha is associated with insulin-mediated suppression of free fatty acids and net lipid oxidation in HIV-infected patients with lipodystrophy. Metabolism 2006, 55: 17-82.
17. Penzak SR., Chuck SK. Management of protease inhibitor-associated hyperlipidemia. Am J Cardiovasc Drugs 2002, 2 (2): 91-106.
18. Saves M, Raffi F, Capeau J et al. Factors related to lipodystrophy and metabolic alterations in patients with human immunodeficiency virus infection receiving highly antiretroviral therapy. Clin Infect Dis 2002; 34 (10): 1396-405.
19. Liang JS, Distler O, Cooper DA et al. HIV protease inhibitors protect apolipoprotein B from degradation by the proteasome: a potential mechanism for protease inhibitor-induced hyperlipidemia. Nat Med. 2001; 7 (12): 1327-1331

20. Purnell JQ, Zambon A, Knopp H et al. Effect of ritonavir on lipids and post-heparin lipase activities in normal subjects. AIDS 2000; 14 (1): 51-57
21. Rhew DC, Bernal M, Aguilar D et al. Association between protease inhibitor use and increased cardiovascular risk in patients infected with human immunodeficiencyvirus: a systematic review. Clin Infect Dis., 2003; 37(7):959-972.
22. F Boccara, S Ederhy, S Janower et al Dossier Athérosclérose et VIH. Risque cardio-vasculaire chez le patient infecté par le VIH. mt cardio 2005 ; 1 : 195-200
23. Capeau J, Girard PM, Katlama C et al. VIH, Doin Edition 2004:46-50.29.
24. Sabin C.A., S.W. Worm, R. Weber et al. Use of nucleoside reverse transcriptase inhibitors and risk of myocardial infarction in HIVinfected patients enrolled in the DAD study: a multicohort collaboration. Lancet 2008, 371 (9622): 1417-1426.
25. Oh J., R.A. Hegele. HIV-associated dyslipidemia : pathogenesis and treatment. Lancet Infect Dis 2007; 7 (12): 787-96