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Metabolic syndrome in HIV-infected middle-aged women on antiretroviral therapy: prevalence and associated factors

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ABSTRACT

Objectives: To determine the prevalence of metabolic syndrome (MetS) and its associated factors in a group of HIV-infected middle-aged women.
Methods: Cross-sectional study including 273 HIV-infected climacteric women of 40–60 years of age under care in two HIV outpatient reference centers in Brazil. Metabolic syndrome diagnosis was based on 2006 International Diabetes Federation criteria. Sociodemographic, clinical and behavioral factors were evaluated as well as HIV infection-related parameters.
Results: Mean age was 47.7 years; 59.1% of women were premenopausal, 91% were on antiretroviral therapy. Current CD4 count was >500 cells/mm^3 in 61.7%, current viral load undetectable in 76.9% of women, and a quarter had previous diagnosis of aids. The prevalence of metabolic syndrome in the subgroup of menopausal women was 46.9%. Univariate analysis showed an association between metabolic syndrome and age ≥50 years ($p = 0.002$), schooling <8 years ($p = 0.003$), post-menopause ($p < 0.001$), body mass index (BMI) >25 kg/m^2 ($p < 0.001$), and FSH ≥40 mIU/mL ($p = 0.002$). In the multivariate analysis only increased BMI (PR = 1.09; 95% CI: 1.05–1.13; $p < 0.001$) and FSH levels ≥40 mIU/mL (PR = 1.66; 95% CI: 1.14–2.40; $p = 0.008$) maintained statistical significance. There was no association between PI use or any other factor related to HIV-infection and MetS in any of the analyses performed.
Conclusion: High BMI and FSH levels compatible with menopause were the only factors associated with MetS in these middle aged HIV-infected women. In the context of well-controlled, early treated HIV infection, traditional rather than HIV-related factors were associated with MetS.

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Introduction

The worldwide implementation of highly active antiretroviral therapy (HAART) for HIV infection resulted in a drastic reduction in morbidity and mortality, as well as in an increase in life expectancy of people living with HIV (PLHIV). HIV infection has acquired characteristics of a controllable chronic disease.[1–3] With the prolonged longevity, the risk of aging-related diseases in PLHIV is higher, even for those individuals with well controlled infection.[2,3]

Metabolic syndrome (MetS) is a useful construct to identify patients in whom there is a greater overall risk of mortality and, specifically, a greater risk of dying from cardiovascular-related causes or diabetes.[4] Increased rates of MetS (33–45%) among PLHIV have been reported by some investigators, while other studies showed rates comparable to those found in the general population (11–26%).[5–16] These differences are due to population heterogeneity across the studies regarding clinical and demographic features, and factors related to HIV infection itself, as well as to the set of criteria used to diagnose MetS.

Factors previously reported to be associated with MetS in HIV-infected populations are high body mass index (BMI), high proportion of central body fat, older age, and reported high calorie, high carbohydrate and high overall sugar intake. With respect to HIV-related factors, high viral load and use of protease inhibitors (PI) have been associated with greater prevalence of MetS.[5–16] In the general population, postmenopausal women are at a greater risk of developing MetS compared to premenopausal women.[17–21] Regarding diagnosis criteria for MetS in a study of PLHIV, low high-density lipoprotein (HDL)-cholesterol was found in 68.5%, and the common profile of MetS was high waist circumference, low HDL-cholesterol and abnormal blood pressure (29.6%).[15]

Nevertheless, the mechanisms underlying MetS and cardiovascular disease in PLHIV remain poorly understood, as is the role of each pathogenic factor and the complex interactions between traditional factors for MetS, HIV infection and its treatment.[5–14] The toxicity profile of antiretroviral drugs has improved immensely over the past 10 years and their efficacy in suppressing the virus is more enduring. Recent data suggest that the immunological recovery and viral suppression promoted by modern antiretroviral therapy (ART) have a favorable cardiovascular effect, approximating the cardiovascular risk of PLHIV to that of the general population.[22,23]

One consequence of the increased life expectancy of PLHIV is the growing number of women living with HIV going through the physical changes of menopausal transition.[17] Despite the viral suppression and immune recovery promoted by modern treatment, aging, together with prolonged exposure to antiretroviral drugs, may increase the risk of MetS in this emerging population.[3] Evaluating the prevalence and particularities of MetS in the population of aging women under modern ART according to their reproductive phase may contribute significantly toward managing cardiovascular risk in this population, a challenge that is increasingly central in the care of PLHIV.

Methods

Study design and participants

For this cross-sectional study, 40 to 60 year-old women were recruited in the referral HIV/AIDS outpatient clinics at the teaching hospital of the University of Campinas (UNICAMP), São Paulo, Brazil and at the Eduardo de Menezes Hospital in Belo Horizonte, Minas Gerais between October 1, 2010 and July 31, 2012. After providing informed consent, women with documented diagnosis of HIV infection according to the Brazilian Ministry of Health algorithm (MS, 2010) were included in the study. Women who had been submitted to oophorectomy and those considered incapable of answering the study questionnaire were excluded. Recruitment and study procedures were undertaken during the routine visits to the participating HIV/AIDS outpatient clinics. Refusal rate was 4% and the main alleged reasons were lack of additional time needed to data collection and blood tests.

Data collection

A structured questionnaire based on an interview conducted in a private setting immediately prior to or following the routine medical visit was completed by the investigator. Demographic and behavioral data were collected as well as data regarding menopause and patient's reproductive cycle. Menopause status was determined by state in relation to menopause, reported by women using the definition of Jaszmann and classified as: premenopausal (women with regular menstrual cycles or menstrual pattern similar to what they had during their reproductive life), perimenopause (women with menstrual cycles in the past 12 months, but with change in menstrual pattern as the previous standards), and postmenopausal (women whose last menstrual period occurred at least 12 months before the interview). Menopausal status in women with previous hysterectomy was confirmed according to the serum levels of follicle stimulating hormone (FSH) on any day and classified as: premenopausal (<10 mIU/mL); menopausal transition (≥10 and <30 mIU/mL); and postmenopausal (≥30 mIU/mL). During the same visit, measurements of waist circumference, blood pressure, weight and height were taken, and the patient's body mass index (BMI) was calculated. Data regarding time between HIV diagnosis and current visit, aids diagnosis, previous and current ART, CD4 counts, and quantitative HIV-1 RNA PCR were abstracted from medical records. CD4 and HIV-1 RNA PCR measurements from the 4-month period containing the study visit were recorded as "current" CD4 and HIV-1 RNA. Blood samples were collected to measure fasting glucose, HDL cholesterol, triglycerides, FSH, TSH, and free T4.

Definition of the metabolic syndrome

Diagnosis of MetS was based on the definition of the International Diabetes Federation (IDF) for South American women, which requires waist circumference ≥80 cm together with two or more of the following factors: triglycerides ≥150 mg/dL, HDL

cholesterol <50 mg/dL, systolic blood pressure ≥130 mmHg or diastolic pressure ≥85 mmHg, fasting glucose ≥100 mg/dL or being under current pharmaceutical treatment for these conditions.

Independent variables

General and HIV-related parameters were included as independent variables to be explored as predictive factors for MetS. General variables were: age (years); skin color (white/other); practice of physical activity in the preceding month (none or up to twice a week/three times a week or more); education (<8 years/≥8 years of formal schooling); family income (≤USD 750/>USD 750); number of people living in the household (≤2/>2); smoker (no or past smoker/present smoker); alcohol consumption (yes/no or has never drunk); menopausal status (pre- or perimenopausal/postmenopausal); weight gain (yes/no); use of hormone therapy (yes/no); self-perception of health (good or excellent/not very good or poor); other chronic diseases (yes/no); BMI (kg/m^2); FSH (mIU/mL); TSH (mIU/L); and free T4 (normal/abnormal). HIV-related variables were: time since diagnosis of HIV infection (years), previous diagnosis of aids (yes/no), on ART (yes/no), ART duration (years), PI use (previous or current, yes/no), current CD4 count (cells/mm^3), current HIV-1 RNA (copies/mL).

Statistical analysis

Calculation of sample size was based on the prevalence of MetS in PLHIV reported from previous studies.[5–16] Considering an alpha error of 0.05 and a beta error of 0.20, the sample size necessary to evaluate MetS was calculated at 242 women.

Associations between independent variables and MetS were explored. Yates chi-square test and Fisher's exact test were used to evaluate categorical variables. Poisson's multiple regression analysis was adjusted in the various models for each independent variables used to evaluate the factors associated with MetS. The variables with a *p*-value ≤0.05 were included in the final model. The method used to select the variables was the backward elimination method in which all the variables are initially included, with those that are not statistically significant being excluded one by one until only those variables with *p*-values <0.05 remain in the final model. The prevalence ratios (PR) and their respective 95% confidence intervals (95% CI) were calculated. The programs used to process and analyze the data were the SPSS software program, version 17.0, and Stata, version 7.

Ethical aspects

The study was approved by the internal review board of the University of Campinas (UNICAMP) and Eduardo de Menezes Hospital, and was conducted by the current version of the Declaration of Helsinki and Resolution 196/12 of the National Council of Ethics in Research (CONEP). This study is part of a broader research project on menopausal symptoms; bone mass; sexual function, and metabolic markers. The relevant approval documents are IRB 407/2010 and CAAE 0313.0.146.000-10.

Results

Two hundred seventy-three HIV-infected climacteric women were included in the study. Detailed demographics and behavioral characteristics and data on general health are shown in Table 1. The mean age was 47.7 years, with most women (64.1%) being between 40 to 50 years old. The majority was premenopausal (59.1%). Only 25.5% had previous diagnosis of AIDS, while 91% were on ART. The mean time since HIV diagnosis was 9.9 years, with a mean of 9.4 years of exposure to ART. The response to treatment was excellent in the majority of cases, as shown by the rate of undetectable viral load in 76.9% and CD4 count over 500 cells/mm^3 in 61.7% of cases.

Table 1 – Population characteristics (*n* = 273).

	n (%), if not otherwise stated
Demographics	
Age (mean ± SD, years)	47.7 ± 5.8
40–49	175 (64.1)
50–60	98 (35.9)
Education, up to 7 years	159 (58.2)
White	109 (39.9)
Family income ≤750 dollars	172 (63.0)
Behavior and lifestyle	
Physical activity ≥3 times/week	59 (21.6)
Smoking, current/in the last year	78 (28.6)
Alcohol consumption, current/in the last year	81 (29.7)
Illicit-drug use, current or past	38 (13.9)
General health indicators	
Self-perception of health as excellent or good	176 (64.5)
Comorbidities	90 (32.9)
BMI ≥ 25 (kg/m^2)	132 (48.3)
Weight gain in the last year	111 (40.6)
HIV infection-related indicators	
Time since HIV diagnosis (mean ± SD, years)	9.9 ± 5.4
Previous aids diagnosis	70 (25.6)
On ART	248 (90.8)
ART duration (mean ± SD, years)	9.4 ± 4.8
PI use, previous or current	145 (53.2)
NNRTI use, previous or current	168 (61.5)
INSTI use, previous or current	9 (3.4)
Current CD4 cell count (cells/mm^3)	
0–100	8 (3)
101–200	12 (4.5)
201–500	84 (30.7)
>500	169 (61.8)
Current HIV-1 PCR (copies/mL)	
<50	212 (76.9)
≥50	(23.1)
Hormonal indicators	
Post-menopause	111 (40.6)
On hormonal therapy	6 (2.1)
FSH <40 (mIU/mL)	155 (56.8)

HIV, human immunodeficiency virus; BMI, body mass index; ART, antiretroviral therapy; FSH, follicle stimulating hormone; PI, protease inhibitor; NNRTI, non-nucleoside analog reverse transcriptase inhibitor; INSTI, integrase inhibitor.

According to the IDF criteria, 120 of 256 participants were diagnosed with MetS, resulting in a prevalence of 46.9%.

With respect to the factors related to the presence of MetS, the univariate analysis (Table 2) showed a statistically significant association with age ≥50 years ($p = 0.002$), schooling <8 years ($p = 0.003$), post-menopause ($p < 0.001$), BMI >25 kg/m^2 ($p < 0.001$) and FSH ≥40 mIU/mL ($p = 0.002$). However, only BMI >25 kg/m^2 (PR = 1.09; 95% CI: 1.05–1.13; $p < 0.001$), and FSH level ≥40 mIU/mL (PR = 1.66; 95% CI: 1.14–2.40; $p = 0.008$) remained independently associated with MetS in the multivariate analysis (Table 3). There was no association between the presence of the MetS and use of protease inhibitors or any other factor related to HIV-infection in any of the analyses performed.

Table 4 shows the prevalence of the different diagnostic criteria for MetS according to the 2006 IDF definitions. Waist circumference ≥80 cm was present in 100% of cases, since that is an essential diagnostic criterion. Other criteria present in this population, in order of frequency, were: HDL <50 mg/dL (56.7%), blood pressure ≥130/85 mmHg (51.3%), triglycerides ≥150 mg/dL (42.8%), and glucose ≥100 mg/dL (24.6%).

Table 2 – Prevalence and associated factors of metabolic syndrome in HIV+ women ($n = 273$, bivariate analysis).

Variables	MetS+ (%)	MetS− (%)	p[a]
Age (years)			0.002
40–49	39.3	60.7	
50–60	60.2	39.8	
Skin color			0.763
Other	48.0	52.0	
White	45.3	54.7	
Physical activity[c]			1.000
0–2 times/week	46.5	53.5	
≥3 times/week	47.3	52.7	
Formal education (years)			0.003
0–7	55.0	45.0	
≥8	35.2	64.8	
Smoking			0.722
No/past	45.9	54.1	
Yes	49.3	50.7	
Alcohol consumption			0.842
No/past	47.5	52.5	
Yes	45.2	54.8	
Menopausal status			<0.001
Pre- or peri-menopause	37.3	62.7	
Post-menopause	61.2	38.8	
Weight gain[c]			0.075
No	41.7	58.3	
Yes	53.8	46.2	
Hormonal therapy[d]			0.189[b]
No	46.2	53.8	
Yes	80.0	20.0	
Self-perception of health[d]			0.861
Excellent/good	47.6	52.4	
Not so good/bad	45.6	54.4	
On ART			0.318
No	34.8	65.2	
Yes	48.1	51.9	
Other chronic diseases[e]			0.596
No	44.3	55.7	
Yes	48.8	51.2	
BMI (kg/m^2)[c]			<0.001
≤25	28.7	71.3	
>25	68.1	31.9	
FSH (mIU/mL)[f]			0.002
<40	37.2	62.8	
≥40	58.7	41.3	
Illicit drugs use			0.311
No	48.4	51.6	
Yes/past	37.8	62.2	
Time since HIV diagnosis (years)[h]			0.681
0–10	48.0	52.0	
>10	44.4	55.6	
ART duration (years)[i]			0.053
0–1	10.0	90.0	
≥2	46.5	53.5	
Current HIV-1 RNA PCR (copies/mL)[g]			0.742
0–50	45.5	54.5	
>50	49.1	50.9	

Discussion

A high prevalence of MetS was found in these middle-aged women living with HIV on ART at two referral services in Brazil between 2010 and 2012. Nevertheless, although high, the MetS rate of 46.9% in the present study is similar to those found in other studies including middle-aged HIV-negative women. Figueiredo Neto et al., using the same IDF criteria, diagnosed MetS in 49.9% of pre- and post-menopausal Brazilian women aged 40–65 years.[24] Oliveira also reported an even higher rate (56.9%) in women over 45 years of age in a rural area of Bahia, a state in northeastern Brazil.[25] Based on the same diagnostic criteria used in the present study, Ford identified MetS in 33% of women in the general population in the United States and in 49% of women aged 50–59 years old.[26] On the other hand, in Austria, Ponholzer et al. reported a lower prevalence: 8.6% in premenopausal women with a median age of 38 years and 32.6% in menopausal women.[27] However, data specifically on MetS in middle aged HIV-infected women are scarce. The population of the present study consisted predominantly of women of 40–50 years of age who had not yet reached menopause, were not at an advanced stage of HIV infection, were under modern ART, and whose immunological status was excellent. In other words, the profile of these women's general and immunological health nears that of the general population. Our finding of a prevalence rate of MetS similar to that reported for the general population in publications both in Brazil and worldwide is in agreement with recent evidence suggesting a "normalization" of health in PLHIV who begin treatment early, have access to adequate treatment and achieve satisfactory immune recovery.[23,28,29]

In our study, the most common diagnostic parameters for MetS were low HDL cholesterol levels and hypertriglyceridemia, whereas abnormal glucose levels were present in only 24.6% of the women with the MetS. Likewise, a relatively higher frequency of hypertriglyceridemia, and low levels of HDL cholesterol have been reported by other investigators in PLHIV in relation to the frequency of the MetS in the general

Table 2 – (*Continued*)

Variables	MetS+ (%)	MetS− (%)	p[a]
Current CD4 cell count (cells/mm³)[j]			0.212
0–199	63.2	36.8	
≥200	45.5	54.5	
Lopinavir use (previous or current)[k]			0.355
Yes	42.3	57.7	
No	50.0	50.0	
Indinavir (previous or current)[l]			0.127
Yes	58.1	41.9	
No	43.5	56.5	

[a] Yates chi-square.
[b] Fisher's exact test.
HIV, human immunodeficiency virus; BMI, body mass index; HAART, highly active antiretroviral therapy; FSH, follicle stimulating hormone.
Missing data:
[c] 1 case.
[d] 2 cases.
[e] 7 cases.
[f] 15 cases.
[g] 10 cases.
[h] 23 cases.
[i] 61 cases.
[j] 6 cases.
[k] 52 cases.
[l] 59 cases.

Table 3 – Factors associated with metabolic syndrome in HIV+ women (multiple regression analysis) (*n* = 240).

Variable	PR 95%	CI	p
BMI (kg/m²)	1.09	1.05–1.13	<0.001
FSH (≥40 mIU/mL)	1.66	1.14–2.40	0.008

PR, prevalence ratio; 95% CI, 95% confidence interval; BMI, body mass index; FSH, follicle stimulating hormone.
Variables considered: age (years); skin color (white/other); physical activity (0–2 times per week/≥3 times per week); education (0–7 years/≥8 years); family income (≤USD 750.00/>USD 750.00); household members (up to 2/>2); smoking (yes/no); alcoholism (yes/no); menopausal status (pre- or peri-menopause/post-menopause); weight gain (yes/no); hormone therapy (yes/no); self-rated health (excellent or good/not so good or bad); On ART (yes/no); other chronic diseases (yes/no); BMI (kg/m²); FSH (<40/≥40); TSH (≤4.5/>4.5); Free T4 (<0.90 or >1.80/0.90 to 1.80); drug use (yes or past/no); type of drug (marijuana, another/crack, Cocaine, Heroin); time since HIV diagnosis (≤10 years/>10 years); lopinavir use, current or previous (yes/no); Indinavir use, current or previous (yes/no); ART duration (≤1 year/>1 year); HIV-1 RNA PCR (≤50/>50); current CD4 cell count (<200/≥200); nadir CD4 (<200/≥200).

Table 4 – Diagnosis of metabolic syndrome – prevalence of each IDF diagnosis criterion in HIV middle-aged women (*n* = 187).

Variables	HIV+ (%)
HDL	
<50 mg/dL	56.7
≥50 mg/dL	43.3
Blood pressure	
<130 × 85 mmHg	48.7
≥130 × 85 mmHg	51.3
Triglycerides	
<150 mg/dL	57.2
≥150 mg/dL	42.8
Glycemia	
<100 mg/dL	75.4
≥100 mg/dL	24.6

HIV, human immunodeficiency virus; HDL, high density lipoprotein.

population.[30] The direct effects of the infection in reducing the HDL fraction of cholesterol and increasing triglyceride levels and the effect of ART on triglycerides are well known and explain the present findings. It is possible that in years to come the progressive improvement in treatment, involving more timely interventions and drugs with little effect on lipids, may change the profile of the diagnostic parameters of the MetS in PLHIV.

In this population of HIV-infected women, those with MetS, compared to those without it, were relatively older, more obese, had poorer education level, and were more likely to be climacteric and to have FSH levels >40 mIU/mL, reflecting estrogen deprivation. Only BMI >25 kg/m² and FSH ≥40 mIU/mL remained as predictors of MetS in the multivariate analysis. Each unit of kg/m² above 25 added to the BMI was associated with a 9% increase in the risk of MetS. Women with FSH ≥40 mIU/mL had a 66% greater risk of having MetS compared to women with FSH <40 mIU/mL. None of the HIV-related characteristics such as disease staging and the duration of infection, exposure to any ART or to PI, immune status, and viral suppression were associated with the presence of MetS in this population.

In the present study, only traditional risk factors were predictors of MetS. The effect of menopause and BMI on the risk of MetS has already been shown in various previous studies and there is strong evidence for the role of these factors as independent predictors of MetS.[17–21,31] In other studies involving PLHIV, traditional risk factors such as age, BMI, weight gain, and dietary patterns were also strong predictors of MetS.[6–11,15,30,32,33]

With respect to HIV-related factors, PI use was found to be marginally associated with MetS in a study conducted by Samaras et al.[33] In that study, however, over 57% of the patients had a clinical diagnosis of lipodystrophy. In this respect, the combination of advanced infection and exposure to more toxic and less effective ARV drugs may have contributed to the development of metabolic alterations that define MetS. The same could be said with respect to the findings of Jericó et al. who reported an increased risk of MetS in patients on ART and on PI compared to treatment-naïve patients. It should also be taken into consideration that the comparison between treatment-naïve patients and patients under ART was not controlled for various confounders associated with HIV infection. In general, in the past observational studies, patients who had not initiated treatment were those in the earliest phase of infection, whose clinical and immune status were better. In the study conducted by Mondy et al., type of ART and time on treatment were not predictors of MetS.[30]

Studies relating ART MetS could be grouped into two phases. Early studies showed an association between ART and dyslipidemia, insulin resistance, and fat redistribution, an association attributed particularly to PIs. On the contrary, more recent studies, beginning with the Strategies for Management of ARV Therapy (SMART) trial, suggested a positive effect of the treatment on metabolism.[34] On the other hand, in the present study, the protective or harmful role of ART could not be investigated adequately because the number of treatment-naïve women was very small (<9%), which limited the statistical power of the analysis. Likewise, the possible influence of other aspects of the infection such as stage of the disease, nadir CD4 count and the patient's current immune and viral status was not confirmed by these results, since the sub-groups of women with advanced uncontrolled disease were small. This limited the statistical power to identify the role of these factors as predictors of MetS. This study was limited by its cross-sectional nature, the scarcity of information concerning the cumulative exposure of the patients to each antiretroviral drug, and the heterogeneity of their therapeutic history. It is still a great challenge to assess the complex effect of ART on metabolic syndrome. Larger prospective studies shall clarify these issues.

Conclusion

The results of the present study show a high prevalence of MetS in middle-aged HIV-infected women; however, the prevalence is similar to that of the general population. The predictive factors of MetS in this population were elevated FSH levels and high BMI, both of which are traditional risk factors for the syndrome. Factors related to HIV infection and its treatment were not associated with MetS in this group of women with access to effective and timely treatment, and whose immune and general health status was good. The present results are in agreement with recent evidence showing that, with access to modern ARV treatment, morbidity and mortality of the HIV-infected patients is similar to that of the general population.

The high prevalence of MetS found in middle-aged HIV-infected women and the current profile of the epidemic, with PLHIV aging, indicate that MetS is indeed an increasingly common problem within the context of clinical management of HIV. In this new phase of the epidemic, it is essential to develop specific strategies for prevention, diagnosis, and treatment of MetS in PLHIV.

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Conflicts of interest

The authors declare no conflicts of interest.

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REFERENCES

1. Palella FJ Jr, Delaney KM, Moorman AC, et al. Declining morbidity and mortality among patients with advanced human immunodeficiency virus infection. HIV Outpatient Study Investigators. N Engl J Med. 1998;338:853–60.
2. Manfredi R, Calza L. HIV infection and AIDS in advanced age. Epidemiological and clinical issues, and therapeutic and management problems. Infez Med. 2004;12:152–73.
3. Deeks SG, Lewin SR, Havlir DV. The end of AIDS: HIV infection as a chronic disease. Lancet. 2013;382:1525–33.
4. Lobo RA. Treatment of the postmenopausal woman: where we are today. In: Lobo RA, editor. Treatment of the postmenopausal woman: basic and clinical aspects. New York: Raven Press; 2007. p. 427–32.
5. Eshtiaghi R, Esteghamati A, Nakhjavani M. Menopause is an independent predictor of metabolic syndrome in Iranian women. Maturitas. 2010;65:262–6.
6. Heidari R, Sadeghi M, Talaei M, Rabiei K, Mohammadifard N, Sarrafzadegan N. Metabolic syndrome in menopausal transition: Isfahan Healthy Heart Program, a population based study. Diabetol Metab Syndr. 2010;2:59.
7. Kim HM, Park J, Ryu SY, Kim J. The effect of menopause on the metabolic syndrome among Korean women: the Korean National Health and Nutrition Examination Survey, 2001. Diabetes Care. 2007;30:701–6.
8. Pandey S, Srinivas M, Agashe S, et al. Menopause and metabolic syndrome: a study of 498 urban women from western India. J Midlife Health. 2010;1:63–9.
9. International Diabetes Federation (IDF). The IDF consensus worldwide definition of the metabolic syndrome. Available at: http://www.idf.org/webdata/docs/IDF_Meta_def_final.pdf [accessed 14.06.14].
10. Lauda LG, Mariath AB, Grillo LP. Metabolic syndrome and its components in HIV-infected individuals. Rev Assoc Med Bras. 2011;57:182–6.
11. Alencastro PR, Fuchs SC, Wolff FH, Ikeda ML, Brandão AB, Barcellos NT. Independent predictors of metabolic syndrome in HIV-infected patients. AIDS Patient Care STDS. 2011;25:627–34.
12. Signorini DJ, Monteiro MC, Andrade MF, Signorini DH, Eyer-Silva WA. What should we know about metabolic syndrome and lipodystrophy in AIDS? Rev Assoc Med Bras. 2012;58:70–5.
13. Krishnan S, Schouten JT, Atkinson B, et al. Metabolic syndrome before and after initiation of ARV therapy in treatment-naive HIV-infected individuals. J Acquir Immune Defic Syndr. 2012;61:381–9.
14. Freitas P, Carvalho D, Souto S, et al. Impact of lipodystrophy on the prevalence and components of metabolic syndrome in HIV-infected patients. BMC Infect Dis. 2011;11:246.
15. Alvarez C, Salazar R, Galindez J, et al. Metabolic syndrome in HIV-infected patients receiving ARV therapy in Latin America. Braz J Infect Dis. 2010;14:256–63.
16. Bonfanti P, De Socio GL, Marconi P, et al. Is metabolic syndrome associated to HIV infection per se? Results from the HERMES study. Curr HIV Res. 2010;8:165–71.
17. Cahn PE, Gatell JM, Squires K, et al. Atazanavir – a once-daily HIV protease inhibitor that does not cause dyslipidemia in

newly treated patients: results from two randomized clinical trials. J Int Assoc Physicians AIDS Care. 2004;3:92–8.
18. Ramírez-Marrero FA, De Jesús E, Santana-Bagur J, Hunter R, Frontera W, Joyner MJ. Prevalence of cardiometabolic risk factors in Hispanics living with HIV. Ethn Dis. 2010;20: 423–8.
19. Van Wijk JP, Cabezas MC. Hypertriglyceridemia, metabolic syndrome, and cardiovascular disease in HIV-infected patients: effects of ARV therapy and adipose tissue distribution. Int J Vasc Med. 2012;2012:201027.
20. Guira O, Tiéno H, Diendéré AE, et al. Features of metabolic syndrome and its associated factors during highly active antiretroviral therapy in Ouagadougou (Burkina Faso). J Int Assoc Provid AIDS Care. 2016;15:159–63.
21. Silva EF, Bassichetto KC, Lewi DS. Lipid profile, cardiovascular risk factors and metabolic syndrome in a group of AIDS patients. Arq Bras Cardiol. 2009;93:113–8.
22. Smith CJ, Ryom L, Weber R, et al. Trends in underlying causes of death in people with HIV from 1999 to 2011 (D:A:D): a multicohort collaboration. Lancet. 2014;384:241–8.
23. Klein DB, Leyden WA, Xu L, et al. Declining relative risk for myocardial infarction among HIV-positive compared with HIV-negative individuals with access to care. Clin Infect Dis. 2015;60:1278–80.
24. Figueiredo Neto JA, Figuerêdo ED, Barbosa JB, et al. Metabolic syndrome and menopause: cross-sectional study in gynecology clinic. Arq Bras Cardiol. 2010;95:339–45.
25. de Oliveira EP, de Souza ML, de Lima M. Prevalence of metabolic syndrome in a semi-arid rural area in Bahia. Arq Bras Endocrinol Metabol. 2006;50:456–65.
26. Ford ES. Prevalence of the metabolic syndrome defined by the International Diabetes Federation among adults in the U.S. Diabetes Care. 2005;28:2745–9.
27. Ponholzer A, Temml C, Rauchenwald M, Marszalek M, Madersbacher S. Is the metabolic syndrome a risk factor for female sexual dysfunction in sexually active women? Int J Impot Res. 2008;20:100–4.
28. Rabasseda X. A report from the Conference on Retroviruses and Opportunistic Infections (CROI) 2015 (February 23–26 – Seattle, Washington, USA). Drugs Today. 2015;51: 209–16.
29. May MT, Gompels M, Delpech V, et al. UK Collaborative HIV Cohort (UK CHIC) Study. Impact on life expectancy of HIV-1 positive individuals of CD^{4+} cell count and viral load response to ARV therapy. AIDS. 2014;28:1193–202.
30. Mondy K, Overton ET, Grubb J, et al. Metabolic syndrome in HIV-infected patients from an urban, midwestern US outpatient population. Clin Infect Dis. 2007;44:726–34.
31. Deibert P, König D, Vitolins MZ, et al. Effect of a weight loss intervention on anthropometric measures and metabolic risk factors in pre- versus postmenopausal women. Nutr J. 2007;6:31.
32. Jericó C, Knobel H, Montero M, et al. Metabolic syndrome among HIV-infected patients: prevalence, characteristics, and related factors. Diabetes Care. 2005;28:132–7.
33. Samaras K, Wand H, Law M, Emery S, Cooper D, Carr A. Prevalence of metabolic syndrome in HIV-infected patients receiving highly active ARV therapy using International Diabetes Foundation and Adult Treatment Panel III Criteria: associations with insulin resistance, disturbed body fat compartmentalization, elevated C-reactive protein, and hypoadiponectinemia. Diabetes Care. 2007;30:113–9.
34. Kelesidis T, Currier JS. Dyslipidemia and cardiovascular risk in human immunodeficiency virus infection. Endocrinol Metab Clin North Am. 2014;43:665–84.