Dyspareunia in HIV positive and negative middle-aged women

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Dyspareunia in HIV positive and negative middle-aged women

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Key messages

- 41.4% of the HIV-positive middle aged women reported dyspareunia.
- Dyspareunia was mainly associated with vaginal dryness and urinary incontinence.
- HIV was not associated with dyspareunia. We hypothesize that it was because women had few HIV-related symptoms.

Short Summary

Cross-sectional study with 178 HIV-negative and 128 HIV-positive women of 40 to 60 years of age. Dyspareunia was common and was associated principally with vaginal dryness and urinary incontinence.

Abstract

Objectives: To evaluate whether dyspareunia is associated with HIV status in menopausal women and also to assess which factors are associated with dyspareunia in a group of HIV-positive menopausal women. Methods: A cross-sectional study was conducted with 178 HIV-negative and 128 HIV-positive women of 40 to 60 years of age. The Short Personal Experiences Questionnaire (SPEQ) was used to collect data. Sociodemographic, clinical, behavioral and reproductive factors were evaluated, as well as factors related to the HIV infection. Dyspareunia was defined as pain during intercourse. A bivariate analysis and Poisson multiple regression analysis were performed. Results: Overall, 41.4% of the HIV-positive women reported dyspareunia compared to 34.8% of the HIV-negative women (p = 0.242). In the HIV-positive women, bivariate analysis revealed an association between dyspareunia and having a steady partner (p = 0.047); the woman's partner having undergone HIV

testing (p = 0.020); vaginal dryness (p<0.001); muscle/joint pain (p=0.021); physical/emotional violence (p=0.049); urinary incontinence (p=0.004); and the use of lamivudine/zidovudine (p=0.048). Poisson multiple regression analysis found an association between dyspareunia and vaginal dryness (PR=1.96, 95%CI: 1.10-3.50, p=0.023) and urinary incontinence (PR=1.86, 95%CI: 1.06-3.27, p=0.031). Conclusion: Dyspareunia was common in this group of HIV-positive women and was associated principally with vaginal dryness and urinary incontinence. The importance of treating dyspareunia within the context of sexual health in this group of women should be emphasized and appropriate management of this issue may reduce the likelihood of lesions on the vaginal wall, which may act as a portal of entry for other infections.

Keywords: HIV; AIDS; dyspareunia; menopause; urogenital atrophy.

Strengths and limitations of this study

Strengths:

- There are few studies on dyspareunia in HIV positive women and almost none in middle-aged ones.
- We have highlighted the importance of vulvovaginal atrophy and its association with dyspareunia in middle-aged HIV positive women.
- We have showed that HIV infection was not significantly associated with dyspareunia, probably because HIV positive women had few HIV related symptoms.
- The results of this study may help physicians to pay attention on vulvovaginal atrophy and its consequences in this group of HIV positive

women.

Limitations:

- It's a cross-sectional design study
- There were some differences in the clinical characteristics of the HIV-positive and HIV-negative women.

Introduction

Dyspareunia or pain during sexual intercourse is one of the most common problems reported by menopausal women. The variation in the frequency of dyspareunia probably reflects many issues including sociocultural aspects, the period of observation during which the condition was evaluated (ever, the past year) and the duration or design of the study under discussion (questionnaire wording, participants). [1]

For women of all ages, the pain caused by dyspareunia often results in distress, impaired sexual functioning and poor sexual enjoyment, difficulty in relationships and a poorer quality of life. In postmenopausal women, dyspareunia may also intensify personal issues related to aging, body image and health. [2]

As with most of the sexual difficulties faced by women at midlife and beyond, dyspareunia is typically considered a consequence of declining ovarian hormone levels and is usually attributed to vaginal atrophy; [3] however, other factors may also be involved. [4] In fact, psychosexual and biological factors (including muscular, endocrine, immune, neurological, vascular and iatrogenic factors) that predispose to, precipitate and perpetuate the condition may interact

to different degrees in the individual woman, contributing to a continuum of symptoms of increasing severity, with the potential to impair sexual intercourse. [5] Age, [6] depression, nervousness and sexual dysfunction in the partner [4,5] are some other factors associated with dyspareunia.

Menopausal women who are HIV-positive may present a unique set of issues that could affect their sexuality. These issues may include the meaning of their illness, their quality of life, HIV transmissibility, and the dilemma of whether or not to disclose the condition to their partner. Florence et al. reported sexual dysfunction to be common in HIV-positive women, principally as a result of their HIV status and of psychological factors that included depression, irritability and anxiety. [7] On the other hand, women with better mental health, a more positive attitude towards living with HIV, a better quality of life, fewer HIV-related symptoms and who had never used injectable drugs were found to have better sexual functioning. [8] A possible role of antiretroviral drugs in causing sexual dysfunction has been a matter of debate. Whereas some studies have suggested that antiretroviral therapy indeed plays a role in sexual function, others have failed to find any such association. [9]

The majority of studies on dyspareunia have failed to deal with factors associated with the HIV infection, a topic yet to be fully investigated in HIV-positive women during the aging process. Therefore, the objectives of the present study were to evaluate whether dyspareunia is associated with HIV status in middle-aged women and to assess the factors associated with dyspareunia in HIV-positive middle-aged women.

Methods

Study design

A cross-sectional study was conducted in which 537 women of 40 to 60 years of age, 273 of whom were HIV-positive and 264 HIV-negative, were screened for inclusion. These women were receiving care at the infectious diseases and HIV outpatient clinics at the Teaching Hospital of the University of Campinas (UNICAMP), at the genital infections and the menopausal outpatient clinics of CAISM/UNICAMP, and at the infectious diseases outpatient clinic of the Eduardo de Menezes Hospital in Belo Horizonte were invited to participate in the study. Of these, 178 HIV- negative women and 128 HIV- positive women had had vaginal intercourse in the previous month and were willing to answer a questionnaire on dyspareunia. These women were then admitted to the study.

The evaluation instrument was based on the Short Personal Experiences Questionnaire (SPEQ). [10,11] Sociodemographic, clinical, behavioral and reproductive characteristics were assessed as well as issues relating to the HIV infection and partner-related factors.

Blood samples were collected at the moment of admission in the present study, and the rapid test was carried out and compared with the gold standard (ELISA and Western blot).

Sample size

Sample size was calculated by estimating the prevalence of sexual dysfunction in HIV-negative menopausal women at 35.9% [12] and the prevalence of sexual dysfunction in HIV-positive women at 60.0%.[13] To enable comparisons to be drawn between the HIV-positive and HIV-negative groups, the number of women required was calculated at 74 per group for an alpha error of 0.05 and a

beta error of 0.20; however, to enable analysis to be made of the HIV-positive group alone, the required number was 188 women (with a difference of 7 percentage points). Since the actual sample size achieved was 128, the absolute difference was 8.5%.

Dependent variable

Dyspareunia was defined as pain during sexual intercourse in accordance with a pain intensity score of 2 or more within a scale of 1 to 6.

Independent variables

The independent variables were dichotomized as follows: HIV status (positive / negative); skin color (white / other); marital status (has a stable partner/ no stable partner); schooling (≤ 7 years / ≥ 8 years); employment (yes: / no); monthly family income (≤ USD750 / > USD750); receives pension (yes / no); smokes (yes / never or past smoker); alcohol use (currently drinks or used to drink / never drank); hot flushes (yes / no); depression (yes / no); vaginal dryness (yes / no); urinary incontinence (yes / no); weight gain (yes / no); muscle and joint pain (yes / no); self-perception of health (excellent or good / poor or very poor); suffers or has already suffered some form of physical or emotional violence (yes / no); has been forced to have intercourse (yes / no); uses statins (yes / no); chronic disease: hypothyroidism (yes / no); LH (<25.7 / ≥ 25.7); age at first sexual intercourse (≤ 19 years / ≥ 20 years); other type of sexual intercourse in the preceding month: active oral sex (yes / no); passive oral sex (yes / no); woman lives with sexual partner (yes / no); menopausal status: (pre- or perimenopausal/ menopausal); number of sexual partners in the

previous year (none / ≥ 1); partner underwent HIV testing (yes / no); quality of life following diagnosis (changed / unchanged); CD4 cell count (<350 / ≥ 350); CD4 cell count nadir (<199; ≥ 200); use of antiretroviral drug 3TC (Lamivudine, Epivir) (yes/ no); use of antiretroviral drug Tenofovir (yes / no); use of antiretroviral drug lamivudine/zidovudine (yes / no); use of antiretroviral drug Efavirenz (yes / no); antiretroviral drug used in the past: lamivudine/zidovudine (yes / no); antiretroviral drug used in the past: Efavirenz (yes/ no).

Statistical analysis

A bivariate analysis was performed in which dyspareunia was considered the dependent variable and analyzed as a function of the independent variables. Pearson's chi square test and the Yates correction were used to compare the groups. [14] The Poisson multiple regression analysis [15] was adjusted in the various models for each one of the independent variables to evaluate the factors associated with the presence of dyspareunia.

Ethics

The study was approved by the internal review board of CAISM/UNICAMP and was conducted in compliance with the current version of the Declaration of Helsinki and with Resolution 196/96 of the Brazilian National Committee for Ethics in Research (CONEP) and its subsequent revisions. This study forms part of a larger study evaluating menopausal symptoms, bone mass, sexual function and metabolic markers. Process: CEP: 407/2010, CAAE 0313.0.146.000-10.

Women who agreed to participate in the study after receiving instructions from the researchers and who signed a free informed consent form were included.

Results

The HIV-positive women were younger and less likely to have a steady partner, to be employed or to have a formal education compared to the HIV-negative women. More than half the HIV-positive women were pre- or perimenopausal. The characteristics of the women interviewed are shown in Table 1.

Overall, 41.4% (n=53) of the HIV-positive women and 34.8% (n=62) of the HIV-negative women reported dyspareunia. There was no association between HIV status and dyspareunia (p=0.242) (data not shown as table). Furthermore, in the multiple regression analysis of the entire sample of HIV-positive and HIV-negative women taken together (n=306), dyspareunia was not associated with HIV status, but was associated with vaginal dryness (PR=2.06, 95%CI: 1.37-3.10, p=0.001) and urinary incontinence (PR=1.68, 95%CI: 1.14-2.46, p=0.008). Predictive variables considered: HIV status (positive / negative); skin color (white / other); marital status (has a stable partner/ no stable partner); schooling (≤ 7 years / ≥ 8 years); employment (yes: / no); monthly family income (≤ R$1.500 / > R$1500); receives pension (yes / no); smokes (yes / never or past smoker); alcohol use (currently drinks or used to drink / never drank); hot flushes (yes / no); depression (yes / no); vaginal dryness (yes / no); urinary incontinence (yes / no); weight gain (yes / no); muscle and joint pain (yes / no); self-perception of health

(excellent or good / poor or very poor); suffers or has already suffered some form of physical or emotional violence (yes / no); has been forced to have intercourse (yes / no); uses statins (yes / no); chronic disease: hypothyroidism (yes / no); LH (<25.7 / ≥ 25.7); age at first sexual intercourse (≤ 19 years / ≥ 20 years); other type of sexual intercourse in the preceding month: active oral sex (yes / no); passive oral sex (yes / no); woman lives with sexual partner (yes / no); menopausal status: (pre- or perimenopausal/ menopausal); number of sexual partners in the previous year (none / ≥ 1).

(Table not presented).

In the HIV-positive group, 91.4% of the women were currently in use of antiretroviral therapy (ART) and, of these, 87% reported using ART regularly (data not presented as table). Approximately 77% of the HIV-positive women had a CD4 cell count nadir >200. The most common way in which HIV had been acquired was by heterosexual transmission, and the average duration of the HIV infection was 9.5 ± 5.6 years (mean ± SD), with a mean duration of therapy of 8.7 years ±4.5 (mean ± SD). A more detailed description of the HIV-infected women is provided in Table 2.

Bivariate analysis revealed an association between dyspareunia in the HIV-positive women and having a steady partner (p=0.047); the woman's partner having undergone HIV testing (p=0.020); vaginal dryness (p<0.001); muscle/joint pain (p=0.021); physical/emotional violence (p=0.049); urinary incontinence (p=0.004); and the use of lamivudine/zidovudine (p=0.048), Table 3.

According to the Poisson multiple regression analysis, the principal factors associated with dyspareunia in the group of HIV-positive women were: vaginal

dryness (PR = 1.96; 95%CI: 1.10- 3.50; p=0.023) and urinary incontinence (PR=1.86; 95%CI: 1.06-3.27; p = 0.031) (Table 4).

Discussion

The objectives of this study were to evaluate whether HIV status was associated with dyspareunia and to assess the factors associated with pain during sexual intercourse in HIV-positive women of 40 to 60 years of age. Information on dyspareunia in HIV positive women is scarce, especially in middle-aged women. To the best of our knowledge, no other studies have been conducted on dyspareunia in HIV-positive women of 40 to 60 years of age. It has been reported that sexual function in HIV-positive women may be driven principally by psychological factors and by HIV status. [13,16] The present study, however, found that in the overall sample of HIV-positive and negative women dyspareunia was not affected by HIV status. This finding is in agreement with the results of another author, who also reported that few women believed HIV in itself to be the cause of any decline in their sexual functioning, since those women had few HIV-related symptoms . [8]

In the present study, more than three-quarters of the HIV-positive patients had a CD4 cell count nadir > 200 and CD4 cell counts > 500 in their last evaluation, reflecting adequate control of the disease. This may partially explain why no association was found between HIV status and dyspareunia. In line with this, another study showed that women with CD4 counts ≤199 cells/μL reported poorer sexual functioning compared to those whose cell count was ≥ 200. [17]

Other studies have shown that CD4 cell count nadir may also have long-term consequences in terms of prognosis and mortality. [18]

Nevertheless, the CD4 cell count nadir and the last CD4 evaluation were not associated with dyspareunia in the present study, probably because of the small number of women with these low values.

The most important factors associated with dyspareunia in the logistic regression analysis, in HIV positive and negative groups, were vaginal dryness and urinary incontinence, both of which are urogenital disorders associated with estrogen deficiency. The association between vaginal dryness and pain during sexual intercourse has been well documented in the literature. [19,20] With respect to the association between urinary incontinence and dyspareunia, the findings of the present study are in agreement with the results published by Salonia et al., who compared 216 women with urinary incontinence to healthy women without any urinary symptoms and found 44% of dyspareunia in women with urinary incontinence. [21] The type of urinary incontinence was not evaluated in the present study. Nevertheless, there is good evidence that the effects of urinary incontinence on sexual functioning are similar irrespective of whether the condition has been classified as stress, urge or mixed incontinence. Urinary incontinence leads to feelings of embarrassment and inadequacy as well as low self-esteem. It may also lead to dyspareunia. [22]

In the bivariate analysis, the fact that the woman's partner had not been tested for HIV was associated with less dyspareunia. It is reasonable to speculate that not knowing her partner's HIV status may in some way "minimize" a woman's concerns regarding transmission and reduce the probability of tension and dyspareunia. [23] Another factor related to the sexual partner that was

associated with an increase in dyspareunia in the bivariate analysis was the woman having a steady partner. One explanation for this finding may lie in the psychological problems generated by the infection itself, which may arise more frequently in stable relationships. [23,24]

Results of the bivariate analysis revealed an association between physical/emotional violence and dyspareunia. Violence is known to be associated with poorer psychological adjustment and adverse sexual health outcomes in women. [25,26] In addition, having muscle pain was associated with dyspareunia in the bivariate analysis. This finding is in line with another study showing that musculoskeletal pain often interferes with sex and may be associated with dyspareunia. [27] A borderline association was found between the use of lamivudine/zidovudine and dyspareunia; however, no explanation for this association was found in the literature.

Some limitations to the present study must be taken into account. First, its cross-sectional design does not permit any conclusions to be drawn with respect to causality. Furthermore, there were some differences in the clinical characteristics of the HIV-positive and HIV-negative women. These differences could be attributed to the fact that the HIV-negative women were selected at specialist outpatient clinics providing care to menopausal women. Nevertheless, multivariate analysis, conducted in a sufficiently large sample of women after controlling for confounding factors, confirmed that HIV infection was not significantly associated with dyspareunia. Good control of the HIV infection and the regular use of antiretroviral therapy by the majority of the women may have brought this group of women closer to the HIV-negative group in terms of their characteristics.

Conclusions

In this study population, HIV infection was not associated with the presence of dyspareunia. The principal factors associated with dyspareunia in HIV-positive women were vaginal dryness and urinary incontinence. These data indicate a need for multidisciplinary care for HIV-positive menopausal women, paying particular attention to ensuring the women's compliance with antiretroviral therapy and offering improved care when these two clinical situations are present to ensure that these women come as close as possible in this respect to HIV-negative women. Greater attention to dyspareunia as a potential component of women's general HIV and sexual care is warranted. A proactive approach to conversations about vulvovaginal atrophy would improve management of dyspareunia and vaginal dryness. In addition to improving the quality of these women's sexual life, we hypothesize that appropriate management of this issue may reduce the likelihood of lesions on the vaginal wall, which may act as a portal of entry for other infections.

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Extra data

The instrument used to collect data is available by emailing

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Table 1– Characteristics of women according to HIV status

Characteristic	Group		
	HIV-infected (%) (n=128)	HIV-uninfected (%) (n=178)	*p* Value
Age (years)			
40 – 44	43.8	24.7	<0,002 #
45 – 49	28.9	29.2	
50 – 54	15.6	23.1	
≥ 55	11.7	23,0	
Race/ethnicity			
White	35.2	47.2	0,047 &
Non-White	64.8	52.8	
Number of deliveries			
Up to 1	25.0	25.4	>0.999 &
≥2	75.0	74.6	
Marital status			
With partner	58.6	87.1	<0,001 &
Without partner	41.4	12.9	
Schooling (years)			
≤7	62.5	40,4	<0,002 #
8-11	23.4	37,1	
≥12	14.1	22,5	
Employment status			

Yes	59.4	71.9	0.030 &
No	40.6	28.1	
Menopausal status			
Premenopausal	39.8	24.7	<0,002 #
Perimenopausal	28.1	21.4	
Postmenopausal	32.1	53.9	
Smoking habit			
Yes/ Former	28,1	15.2	0,009 &
No	71,9	84.8	
Physical activity			
Up to 2 times/week	77.3	74.2	0,614 &
≥3 times/week	22.7	25.8	

* Sample of women with partner and information on occurrence or not of dispareunia in the last month

Pearson's Chi-square; & Yates's Chi-square

Table 2 – Characteristics associated to HIV status associated with dyspareunia in women with sexual partner in the month before the interview (n=128)

Characteristics	N	%
Nadir CD4 levels (a)		
0 – 100	18	14.5
101 – 200	10	8.1
201 – 500	62	50.0
> 500	34	27.4
Last CD4 levels (a)		
0 – 100	5	4.0
101 – 200	1	0.8
201 – 500	43	34.7
> 500	75	60.5
Total	**124**	**100.0**
HIV risk factor for acquisition		
heterosexual *acquisition*	97	75.8

Illicit drug use	3	2.3
blood transfusion	2	1.6
Não sabe/ Não respondeu	26	20.3
Total	**128**	**100.0**
Use of TARV		
Yes	117	91.4
No	11	8.6
Total	**128**	**100.0**
HIV duration of infection (n=125) (years)	Mean: 9.5	SD: 5.06
Duration of HIV therapy (n=93) (years)	Mean: 8.7	SD: 4.47

(a) Missing information

Table 3 – Factors associated with dyspareunia (score ≥2) in middle-aged HIV positive women: bivariate analysis

Variable	N	Dyspareunia% Score≥2	Score<2	p *
Marital status				**0.047**
Married/live together	75	49.3	50.7	
Don´t live together	53	30.2	69.8	
Did partner have HIV test?				**0.020**
Yes	88	50.0	50.0	
No	27	22.2	77.8	
Vaginal dryness				**<0.001**
Yes	53	58.5	41.5	
No	71	26.8	73.2	
Muscular / articular pain				**0.021**
Yes	83	49.4	50.6	
No	45	26.7	73.3	
Physical/ Emotional violence				**0,049**

Yes	128	55.5	44.5	
No	174	32.8	67.2	
Urinary Incontinence				
				0,004
Yes	41	61.0	39.0	
No	87	32.2	67.8	
Use of biovir				**0.048**
Yes	57	29.8	70.2	
No	63	49.2	50.8	

Predictive variables considered: skin color (white / other); marital status (has a stable partner/ no stable partner); schooling (≤ 7 years / ≥ 8 years); employment (yes: / no); monthly family income (≤ R$1.500 / > R$1500); receives pension (yes / no); smokes (yes / never or past smoker); alcohol use (currently drinks or used to drink / never drank); hot flushes (yes / no); depression (yes / no); vaginal dryness (yes / no); urinary incontinence (yes / no); weight gain (yes / no); muscle and joint pain (yes / no); self-perception of health (excellent or good / poor or very poor); suffers or has already suffered some form of physical or emotional violence (yes / no); has been forced to have intercourse (yes / no); uses statins (yes / no); chronic disease: hypothyroidism (yes / no); LH (<25.7 / ≥ 25.7); age at first sexual intercourse (≤ 19 years / ≥ 20 years); other type of sexual intercourse in the preceding month: active oral sex (yes / no); passive oral sex (yes / no); woman lives with sexual partner (yes / no); menopausal status: (pre- or perimenopausal/ menopausal); number of sexual partners in the previous year (none / ≥ 1); partner underwent HIV testing

(yes / no); quality of life following diagnosis (changed / unchanged); CD4 cell count (<350 / ≥ 350); CD4 cell count nadir (<199; ≥ 200); use of antiretroviral drug 3TC (Lamivudine, Epivir) (yes/ no); use of antiretroviral drug Tenofovir (yes / no); use of antiretroviral drug Lamivudine/zidovudine (yes / no); use of antiretroviral drug Efavirenz (yes / no); antiretroviral drug used in the past: Lamivudine/zidovudine (yes / no); antiretroviral drug used in the past: Efavirenz (yes/ no).

Tabela 4 – Variables associated with dyspareunia in HIV positive women with sexual partner in the month before the interview. Poisson multiple regression [n=124]

Variable	PR	95%CI	p-value
Vaginal dryness	1.96	1.10 – 3.50	**0.023**
Urinary incontinence	1.86	1.06 – 3.27	**0.031**

PR: prevalence ratio; CI 95%: 95% confidence interval; p: p-value

Predictive variables considered: skin color (white / other); marital status (has a stable partner/ no stable partner); schooling (≤ 7 years / ≥ 8 years); employment (yes: / no); monthly family income (≤ R$1.500 / > R$1500); receives pension (yes / no); smokes (yes / never or past smoker); alcohol use (currently drinks or used to drink / never drank); hot flushes (yes / no); depression (yes / no); vaginal dryness (yes / no); urinary incontinence (yes / no); weight gain (yes / no); muscle and joint pain (yes / no); self-perception of health (excellent or good / poor or very poor); suffers or has already suffered some form of physical or emotional violence (yes / no); has been forced to have intercourse (yes / no); uses statins (yes / no); chronic disease: hypothyroidism (yes / no); LH (<25.7 / ≥ 25.7); age at first sexual intercourse (≤ 19 years / ≥ 20 years); other type of sexual intercourse in the preceding month: active oral sex (yes / no); passive oral sex (yes / no); woman lives with sexual partner (yes / no); menopausal status: (pre- or perimenopausal/ menopausal); number of sexual partners in the previous year (none / ≥ 1); partner underwent HIV testing (yes / no); quality of life following diagnosis (changed / unchanged); CD4 cell count (<350 / ≥ 350); CD4 cell count nadir (<199; ≥ 200); use of antiretroviral drug 3TC (Lamivudine, Epivir) (yes/ no); use of antiretroviral drug Tenofovir (yes / no); use of antiretroviral drug

Lamivudine/zidovudine (yes / no); use of antiretroviral drug Efavirenz (yes / no); antiretroviral drug used in the past: Lamivudine/zidovudine (yes / no); antiretroviral drug used in the past: Efavirenz (yes/ no).

checklist **Dyspareunia in HIV positive and negative middle-aged women**

	Item No	Recommendation
okTitle and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found
Introduction		
Ok background/rationale	2	Explain the scientific background and rationale for the investigation being reported
Ok Objectives	3	State specific objectives, including any prespecified hypotheses
Methods		
Ok Study design	4	Present key elements of study design early in the paper
Ok Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection
Ok Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case
Ok Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
Ok Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group
Ok Bias	9	Describe any efforts to address potential sources of bias
Ok Study size	10	Explain how the study size was arrived at
Ok Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
Ok Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding
		(*b*) Describe any methods used to examine subgroups and interactions
		(*c*) Explain how missing data were addressed
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy
		(*e*) Describe any sensitivity analyses

Continued on next page

Results		
Ok Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed
		(b) Give reasons for non-participation at each stage
		(c) Consider use of a flow diagram
Ok Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders
		(b) Indicate number of participants with missing data for each variable of interest
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)
Ok Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time
		Case-control study—Report numbers in each exposure category, or summary measures of exposure
		Cross-sectional study—Report numbers of outcome events or summary measures
Ok Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included
		(*b*) Report category boundaries when continuous variables were categorized
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Ok Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses
Discussion		
Ok Key results	18	Summarise key results with reference to study objectives
Ok Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias
Ok Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
Ok Generalisability	21	Discuss the generalisability (external validity) of the study results
Other information		
Ok Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Dyspareunia in HIV positive and negative middle-aged women: a cross sectional study

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Dyspareunia in HIV positive and negative middle-aged women: a cross – sectional study

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Abstract

Objectives: To evaluate whether dyspareunia is associated with HIV status in menopausal women and also to assess which factors are associated with dyspareunia in a group of HIV-positive menopausal women. Methods: A cross-sectional study was conducted with 178 HIV-negative and 128 HIV-positive women of 40 to 60 years of age. The Short Personal Experiences Questionnaire (SPEQ) was used to collect data. Sociodemographic, clinical, behavioral and reproductive factors were evaluated, as well as factors related to the HIV infection. Dyspareunia was defined as pain during intercourse. A bivariate analysis and Poisson multiple regression analysis were performed. Results: Overall, 41.4% of the HIV-positive women reported dyspareunia compared to 34.8% of the HIV-negative women (p = 0.242). In the HIV-positive women, bivariate analysis revealed an association between dyspareunia and having a steady partner (p = 0.047); the woman's partner having undergone HIV testing (p = 0.020); vaginal dryness (p<0.001); muscle/joint pain (p=0.021); physical/emotional violence (p=0.049); urinary incontinence (p=0.004); and the use of lamivudine/zidovudine (p=0.048). Poisson multiple regression analysis found an association between dyspareunia and vaginal dryness (PR=1.96, 95%CI: 1.10-3.50, p=0.023) and urinary incontinence (PR=1.86, 95%CI: 1.06-3.27, p=0.031). Conclusion: Dyspareunia was common in this group of HIV-positive women and was associated principally with vaginal dryness and urinary incontinence. The importance of treating dyspareunia within the context of sexual health in this group of women should be emphasized and appropriate management of this issue may reduce the likelihood of lesions on the vaginal wall, which may act as a portal of entry for other infections.

Keywords: HIV; AIDS; dyspareunia; menopause; urogenital atrophy.

Strengths and limitations of this study

Strengths:

- We have not found studies on dyspareunia in HIV positive women.
- We have highlighted the importance of vulvovaginal atrophy and its association with dyspareunia in middle-aged HIV positive women.
- We have showed that HIV infection was not significantly associated with dyspareunia, probably because HIV positive women had few HIV related symptoms.
- The results of this study may help physicians to pay attention on vulvovaginal atrophy and its consequences in this group of HIV positive women.

Limitations:

- It's a cross-sectional design study
- There were some differences in the clinical characteristics of the HIV-positive and HIV-negative women.

Key messages

- 41.4% of the HIV-positive middle aged women reported dyspareunia.
- Dyspareunia was mainly associated with vaginal dryness and urinary incontinence.
- HIV was not associated with dyspareunia. We hypothesize that it was because HIV positive women had good immunovirological status.

Short Summary

Cross-sectional study with 178 HIV-negative and 128 HIV-positive women of 40 to 60 years of age. Dyspareunia was common and was associated principally with vaginal dryness and urinary incontinence.

Introduction

Dyspareunia is defined as persistent or recurrent genital pain that occurs just before, during or after intercourse. It is one of the most common problems reported by menopausal women. The variation in the frequency of dyspareunia probably reflects many issues including sociocultural aspects, the period of observation during which the condition was evaluated (ever, the past year) and the duration or design of the study under discussion (questionnaire wording, participants). [1]

For women of all ages, the pain caused by dyspareunia often results in distress, impaired sexual functioning and poor sexual enjoyment, difficulty in relationships and a poorer quality of life. In postmenopausal women, dyspareunia may also intensify personal issues related to aging, body image and health. [2]

As with most of the sexual difficulties faced by women at midlife and beyond, dyspareunia is typically considered a consequence of declining ovarian hormone levels and is usually attributed to vaginal atrophy; [3] however, other factors may also be involved. [4] In fact, psychosexual and biological factors (including muscular, endocrine, immune, neurological, vascular and iatrogenic factors) that predispose to, precipitate and perpetuate the condition may interact to different degrees in the individual woman, contributing to a continuum of

symptoms of increasing severity, with the potential to impair sexual intercourse[5]. Age, [6] depression, anxiety and sexual dysfunction in the partner [4,5] are some other factors associated with dyspareunia. It seems that cognitive-emotional variables (catastrophization, depression, anxiety) are significant predictors of dyspareunia and relationship adjustment variables were inversely associated with pain severity[7] Findings also suggest that dyspareunia impacts not only the psychosexual adjustment of affected women but also that of their partners.[8]

Menopausal women who are HIV-positive may present a unique set of issues that could affect their sexuality. These issues may include the meaning of their illness, their quality of life, HIV transmissibility, and the dilemma of whether or not to disclose the condition to their partner. Florence et al. reported sexual dysfunction to be common in HIV-positive women, principally as a result of their HIV status and of psychological factors that included depression, irritability and anxiety. [9] On the other hand, women with better mental health after HIV diagnosis, a more positive attitude towards living with HIV, a better quality of life, fewer HIV-related symptoms and who had never used injectable drugs were found to have better sexual functioning. [10] A possible role of antiretroviral drugs in causing sexual dysfunction has been a matter of debate. Whereas some studies have suggested that antiretroviral therapy indeed plays a role in sexual function, others have failed to find any such association. [11]

The majority of studies on dyspareunia have failed to deal with factors associated with the HIV infection, a topic yet to be fully investigated in HIV-positive women during the aging process. Therefore, the objectives of the present study were to evaluate whether dyspareunia is associated with HIV

status in middle-aged women and to assess the factors associated with dyspareunia in HIV-positive middle-aged women.

Methods

Study design

A cross-sectional study was conducted in which 537 women of 40 to 60 years of age, 273 of whom were HIV-positive and 264 HIV-negative were screened for inclusion. Patients were recruited at the infectious diseases and HIV outpatient clinics (HIV positive women) and at the menopausal ambulatory care (HIV negative women), both at the Teaching Hospital of the University of Campinas (UNICAMP). Patients were also invited to participate at the infectious diseases outpatient public clinic (HIV positive women)in Belo Horizonte Of these, 178 HIV- negative women and 128 HIV- positive women had had vaginal intercourse in the previous month and were willing to answer a questionnaire on dyspareunia. These women were then admitted to the study.

For inclusion in the HIV-positive group, laboratory confirmation of the women's seropositive status by one of the recommended tests (ELISA or Western Blot) was required (all of them had it), while the women recruited to the HIV-negative group had to have tested negative. The blood samples tests of HIV negative and positive women were collected at the moment of admission in the present study (FSH, LH and TSH for all, ELISA or Western Blot HIV tests for HIV negative women and Viral load and CD4 cells for HIV positive women . Exclusion criteria consisted of nursing mothers, bilaterally oophorectomized women and those unable to answer the questionnaire. The evaluation

instrument was the Short Personal Experiences Questionnaire (SPEQ). [12,13] Sociodemographic, clinical, behavioral and reproductive characteristics were assessed as well as issues relating to the HIV infection and partner-related factors.

Dependent variable

The dependent variable dyspareunia, defined as pain during sexual intercourse, was graded from 1 to 6, where 1 referred to the absence of pain and 6 to maximum pain. A score of less than 2 was considered to represent the absence of dyspareunia and a score of 2 or more to represent the presence of dyspareunia. [12,13,14]

Independent variables

The independent variables were dichotomized as follows: HIV status (positive / negative); skin color (white / other); marital status (has a stable partner/ no stable partner); schooling (≤ 7 years / ≥ 8 years); employment (yes: / no); monthly family income (≤ USD750 / > USD750); receives pension (yes / no); smokes (yes / never or past smoker); alcohol use (currently drinks or used to drink / never drank); hot flushes (yes / no); depression (yes / no); vaginal dryness (yes / no); urinary incontinence (yes / no); weight gain (yes / no); muscle and joint pain (yes / no); self-perception of health (excellent or good / poor or very poor); suffers or has already suffered some form of physical or emotional violence (yes / no); has been forced to have intercourse (yes / no); uses statins (yes / no); chronic disease: hypothyroidism (yes / no);

FSH (<40/≥40), LH (<25.7 / ≥ 25.7); age at first sexual intercourse (≤ 19 years / ≥ 20 years); other type of sexual intercourse in the preceding month: giving oral sex (yes / no); receiving oral sex (yes / no); woman lives with sexual partner (yes / no);; number of sexual partners in the previous year (none / ≥ 1); partner underwent HIV testing (yes / no); quality of life following diagnosis (changed / unchanged); CD4 cell count (<350 / ≥ 350); CD4 cell count nadir (<199; ≥ 200); use of antiretroviral drug 3TC (Lamivudine, Epivir) (yes/ no); use of antiretroviral drug Tenofovir (yes / no); use of antiretroviral drug lamivudine/zidovudine (yes / no); use of antiretroviral drug Efavirenz (yes / no); antiretroviral drug used in the past: lamivudine/zidovudine (yes / no); antiretroviral drug used in the past: Efavirenz (yes/ no). Menopausal status was classified as premenopausal, perimenopausal or postmenopausal. Women were considered premenopausal if they continued to have regular menstrual cycles similar to those present during the woman's reproductive life. They were considered to be in the perimenopause if their menstrual cycles were irregular and they had been amenorrheic for less than 12 months. Finally, women were classified as postmenopausal if they had been amenorrheic for 12 months or more.[15] Data on physical activity was obtained through two questions: Do you practice physical exercise or participate in sports every week? How often in a week do you practice physical exercise or participate in sports?. It was classified in up two times a week or 3 or more times a week. Vaginal lubrication during sexual activity was graded from 1 to 6, where 1 referred to the absence of lubrication and 6 to maximum lubrication. This was dichotomized into 4 or less or more than 4.

Statistical analysis

A bivariate analysis was performed in which dyspareunia was considered the dependent variable (dyspareunia) and analyzed as a function of the independent variables. Pearson's chi square test and the Yates correction were used to compare the groups. [16] The Poisson multiple regression analysis [17] was adjusted in the various models for each one of the independent variables to evaluate the factors associated with the presence of dyspareunia.

Ethics

The study was approved by the internal review board of CAISM/UNICAMP and was conducted in compliance with the current version of the Declaration of Helsinki and with Resolution 196/96 of the Brazilian National Committee for Ethics in Research (CONEP) and its subsequent revisions. This study forms part of a larger study evaluating menopausal symptoms, bone mass, sexual function and metabolic markers. Process: CEP: 407/2010, CAAE 0313.0.146.000-10.

Women who agreed to participate in the study after receiving instructions from the researchers and who signed a free informed consent form were included.

Results

The HIV-positive women were younger and less likely to have a steady partner, to be employed or to have a formal education compared to the HIV-negative women. More than half the HIV-positive women were pre- or perimenopausal. The characteristics of the women interviewed are shown in Table 1.

Overall, 41.4% (n=53) of the HIV-positive women and 34.8% (n=62) of the HIV-negative women reported dyspareunia. There was no association between HIV status and dyspareunia (p=0.242). Furthermore, in the

multiple regression analysis of the entire sample of HIV-positive and HIV-negative women taken together (n=306), dyspareunia was not associated with HIV status, but was associated with vaginal dryness (PR=2.06, 95%CI: 1.37-3.10, p=0.001) and urinary incontinence (PR=1.68, 95%CI: 1.14-2.46, p=0.008).

In the HIV-positive group, 91.4% of the women were currently in use of antiretroviral therapy (ART) and, of these, 87% reported using ART regularly (data not presented as table). Approximately 77% of the HIV-positive women had a CD4 cell count nadir >200. The most common way in which HIV had been acquired was by heterosexual transmission, and the average duration of the HIV infection was 9.5 ± 5.6 years (mean ± SD), with a mean duration of therapy of 8.7 years ±4.5 (mean ± SD). A more detailed description of the HIV-infected women is provided in Table 2.

Bivariate analysis revealed an association between dyspareunia in the HIV-positive women and having a steady partner (p=0.047); the woman's partner having undergone HIV testing (p=0.020); vaginal dryness (p<0.001); muscle/joint pain (p=0.021); physical/emotional violence (p=0.049); urinary incontinence (p=0.004); and the use of lamivudine/zidovudine (p=0.048), Table 3.

According to the Poisson multiple regression analysis, the principal factors associated with dyspareunia in the group of HIV-positive women were: vaginal dryness (PR = 1.96; 95%CI: 1.10- 3.50; p=0.023) and urinary incontinence (PR=1.86; 95%CI: 1.06-3.27; p = 0.031) (Table 4).

Discussion

The objectives of this study were to evaluate whether HIV status was associated with dyspareunia and to assess the factors associated with pain during sexual intercourse in HIV-positive women of 40 to 60 years of age. The calculated number of women required for the sample size was at 74 per group[14]; however, to enable analysis of the HIV-positive group alone, the required number was 188 women[18]. Since the actual sample size achieved was 128, the absolute difference was 8.5%, acceptable since it is less than 10%. Information on dyspareunia in HIV positive women is scarce, especially in middle-aged women. To the best of our knowledge, no other studies have been conducted on dyspareunia in HIV-positive women. It has been reported that sexual function in HIV-positive women may be driven principally by psychological factors and otherproblems related to HIV infection. [18,19] The present study, however, found that in the overall sample of HIV-positive and negative women dyspareunia was not affected by HIV status. This finding is in agreement with the results of another author, who also reported that few women believed HIV in itself to be the cause of any decline in their sexual functioning, since those women had good immunovirological status [10] One supposes that results would be different in a sample of women without a good HIV control. In the present study, more than three-quarters of the HIV-positive patients had a CD4 cell count nadir > 200 and CD4 cell counts > 500 in their last evaluation, thus reflecting adequate control of the disease. This may partially explain why no association was found between HIV status and dyspareunia. In line with this, another study showed that women with CD4 counts ≤199 cells/μL reported poorer sexual functioning compared to those whose cell count was ≥ 200. [20]

Other studies have shown that CD4 cell count nadir may also have long-term consequences in terms of prognosis and mortality. [21]

Nevertheless, the CD4 cell count nadir and the last CD4 evaluation were not associated with dyspareunia in the present study, probably because of the small number of women with these low values.

The most important factors associated with dyspareunia in the logistic regression analysis, in HIV positive and negative groups analyzed together and in the HIV group analysis were vaginal dryness and urinary incontinence, both of which are urogenital disorders associated with estrogen deficiency. The association between vaginal dryness and pain during sexual intercourse has been well documented in the literature, in addition to its consequence on vulvovaginal health. [22,23,24] With respect to the association between urinary incontinence and dyspareunia, the findings of the present study are in agreement with the results published by Salonia et al., evaluated 216 women with urinary incontinence and found 44% of dyspareunia in these women. [25]

The type of urinary incontinence was not evaluated in the present study. Nevertheless, there is good evidence that the effects of urinary incontinence on sexual functioning are similar irrespective of whether the condition has been classified as stress, urge, mixed incontinence[26] or even intersticial cystitis[27]

Urinary incontinence is associated with feelings of embarrassment and inadequacy as well as low self-esteem. It may also be associated to dyspareunia. [25]

Factors associated with dyspareunia in HIV positive women:

In the bivariate analysis, the fact that the woman's partner had not been tested for HIV was associated with less dyspareunia. It is reasonable to speculate that

not knowing her partner's HIV status may in some way "minimize" a woman's concerns regarding transmission and reduce the probability of tension and dyspareunia. [28] Another factor related to the sexual partner that was associated with an increase in dyspareunia in the bivariate analysis was the woman having a steady partner, although this association was borderline,. One explanation for this finding may lie in the psychological problems generated by the infection itself, which may arise more frequently in stable relationships. [28,29] As one has not controlled for frequency of intercourse, one thought is dyspareunia due a lower frequency of intercourse rather than quality of the relationship. Results of the bivariate analysis revealed an association between physical/emotional violence and dyspareunia. Violence is known to be associated with poorer psychological adjustment and adverse sexual health outcomes in women. [30,31] In addition, having muscle pain was associated with dyspareunia in the bivariate analysis. This finding is in line with another study showing that musculoskeletal pain often interferes with sex and may be associated with dyspareunia. [32] A borderline association was found between the use of lamivudine/zidovudine and dyspareunia; however, no explanation for this association was found in the literature. One may hypothesize that dyspareunia in these women could be due depression side effects of these drugs.

Some limitations to the present study must be taken into account. First, its cross-sectional design does not permit any conclusions to be drawn with respect to causality. It is also important to note that it was a clinical sample. So, the results found in the present study may not be extrapolated to the general

population. Furthermore, there were some differences in the clinical characteristics of the HIV-positive and HIV-negative women. These differences could be attributed to the fact that the HIV-negative women were selected at specialist outpatient clinics providing care to menopausal women. By selecting HIV positive women also in menopausal outpatient care, maybe groups would be similar. Nevertheless, multivariate analysis, conducted in a sufficiently large sample of women after controlling for confounding factors, confirmed that HIV infection was not significantly associated with dyspareunia. Good control of the HIV infection and the regular use of antiretroviral therapy by the majority of the women may have brought this group of women closer to the HIV-negative group in terms of their characteristics.

Conclusions

In this study population, HIV infection was not associated with the presence of dyspareunia. The principal factors associated with dyspareunia in HIV-positive women were vaginal dryness and urinary incontinence. These data indicate a need for multidisciplinary care for HIV-positive menopausal women, paying particular attention to ensuring the women's compliance with antiretroviral therapy and offering improved care when these two clinical situations are present to ensure that these women come as close as possible in this respect to HIV-negative women. Greater attention to dyspareunia as a potential component of women's general HIV and sexual care is warranted. A proactive approach to conversations about vulvovaginal atrophy would improve management of dyspareunia and vaginal dryness. In addition to improving the quality of these women's sexual life, we hypothesize that appropriate

management of this issue may reduce the likelihood of lesions on the vaginal wall, which may act as a portal of entry for other infections.

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Conflicts of Interest exist for any of the authors.

Extra data

We have used a questionnaire to collect data for the present study.

The instrument used to collect data is available by emailing

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Table 1– Some characteristics of women according to HIV status

Characteristic	Group HIV-infected (%) (n=128)	HIV-uninfected (%) (n=178)	*p* Value
Age (years)			
40 – 44	43.8	24.7	<0.002[1]
45 – 49	28.9	29.2	
50 – 54	15.6	23.1	
≥ 55	11.7	23,0	
Skin color			
White	35.2	47.2	0.047 [2]
Non-White	64.8	52.8	
Number of deliveries			
Up to 1	25.0	25.4	>0.999[2]
≥2	75.0	74.6	
Marital status			
With partner	58.6	87.1	<0.001[2]
Without partner	41.4	12.9	
Schooling (years)			
≤7	62.5	40,4	<0.002[1]
8-11	23.4	37,1	
≥12	14.1	22,5	
Employment status			
Yes	59.4	71.9	0.030[2]
No	40.6	28.1	
Menopausal status			
Premenopausal	39.8	24.7	<0.002[1]
Perimenopausal	28.1	21.4	
Postmenopausal	32.1	53.9	
Current smoking t			
Yes/ Former	28,1	15.2	0.009[2]
No	71,9	84.8	
Physical activity			
Up to 2 times/week	77.3	74.2	0.614[2]
≥3 times/week	22.7	25.8	

[1]Pearson's Chi-square; & Yates's Chi-square

Table 2 – Characteristics associated to HIV status associated with dyspareunia in women with sexual partner in the month before the interview (n=128)

Characteristics	**N**	**%**
HIV duration of infection (n=125) (years)	Mean: 9.5	SD: 5.06
Duration of HIV therapy (n=93) (years)	Mean: 8.7	SD: 4.47
Nadir CD4 levels (a)		
0 – 100	18	14.5
101 – 200	10	8.1
201 – 500	62	50.0
Last CD4 levels (a)		
0 – 100	5	4.0
101 – 200	1	0.8
201 – 500	43	34.7
> 500	75	60.5
Total	**124**	**100.0**
HIV risk factor for acquisition		
heterosexual acquisition	97	75.8
Illicit drug use	3	2.3
blood transfusion	2	1.6
	26	20.3

Total	**128**	**100.0**
Use of TARV		
Yes	117	91.4
No	11	8.6
Total	**128**	**100.0**

(a) Missing information

Table 3 – Factors associated with dyspareunia (score ≥2) in middle-aged HIV positive women: bivariate analysis

Variable	n	Dyspareunia% Score≥2	Score<2	p
Marital status				**0.047**
Married/live together	75	49.3	50.7	
Don´t live together	53	30.2	69.8	
Did partner have HIV test?				**0.020**
Yes	88	50.0	50.0	
No	27	22.2	77.8	
Vaginal dryness				**<0.001**
Yes	53	58.5	41.5	
No	71	26.8	73.2	
Muscular / articular pain				**0.021**
Yes	83	49.4	50.6	
No	45	26.7	73.3	
Physical/ Emotional violence				**0.049**
Yes	128	55.5	44.5	
No	174	32.8	67.2	
Urinary Incontinence				**0.004**
Yes	41	61.0	39.0	
No	87	32.2	67.8	
Use of biovir				**0.048**
Yes	57	29.8	70.2	
No	63	49.2	50.8	

Table 4 – Variables associated with dyspareunia in HIV positive women with sexual partner in the month before the interview. Poisson multiple regression [n=124]

Variable	PR	95%CI	p-value
Vaginal dryness	1.96	1.10 – 3.50	**0.023**
Urinary incontinence	1.86	1.06 – 3.27	**0.031**

PR: prevalence ratio; CI 95%: 95% confidence interval; p: p-value

Dyspareunia in HIV positive and negative middle-aged women: a cross – sectional study

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Key messages

- 41.4% of the HIV-positive middle aged women reported dyspareunia.
- Dyspareunia was mainly associated with vaginal dryness and urinary incontinence.
- HIV was not associated with dyspareunia. We hypothesize that it was because HIV positive women had good immunovirological status~~few HIV-related symptoms~~.

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Short Summary

Cross-sectional study with 178 HIV-negative and 128 HIV-positive women of 40 to 60 years of age. Dyspareunia was common and was associated principally with vaginal dryness and urinary incontinence.

Abstract

Objectives: To evaluate whether dyspareunia is associated with HIV status in menopausal women and also to assess which factors are associated with dyspareunia in a group of HIV-positive menopausal women. Methods: A cross-sectional study was conducted with 178 HIV-negative and 128 HIV-positive women of 40 to 60 years of age. The Short Personal Experiences Questionnaire (SPEQ) was used to collect data. Sociodemographic, clinical, behavioral and reproductive factors were evaluated, as well as factors related to the HIV infection. Dyspareunia was defined as pain during intercourse. A bivariate analysis and Poisson multiple regression analysis were performed. Results: Overall, 41.4% of the HIV-positive women reported dyspareunia compared to 34.8% of the HIV-negative women (p = 0.242). In the HIV-positive

women, bivariate analysis revealed an association between dyspareunia and having a steady partner (p = 0.047); the woman's partner having undergone HIV testing (p = 0.020); vaginal dryness (p<0.001); muscle/joint pain (p=0.021); physical/emotional violence (p=0.049); urinary incontinence (p=0.004); and the use of lamivudine/zidovudine (p=0.048). Poisson multiple regression analysis found an association between dyspareunia and vaginal dryness (PR=1.96, 95%CI: 1.10-3.50, p=0.023) and urinary incontinence (PR=1.86, 95%CI: 1.06-3.27, p=0.031). Conclusion: Dyspareunia was common in this group of HIV-positive women and was associated principally with vaginal dryness and urinary incontinence. The importance of treating dyspareunia within the context of sexual health in this group of women should be emphasized and appropriate management of this issue may reduce the likelihood of lesions on the vaginal wall, which may act as a portal of entry for other infections.

Keywords: HIV; AIDS; dyspareunia; menopause; urogenital atrophy.

Strengths and limitations of this study

Strengths:

- We have not found studies on dyspareunia in HIV positive women.
- ~~There are few studies on dyspareunia in HIV positive women and almost none in middle-aged ones.~~
- We have highlighted the importance of vulvovaginal atrophy and its association with dyspareunia in middle-aged HIV positive women.
- We have showed that HIV infection was not significantly associated with dyspareunia, probably because HIV positive women had few HIV related symptoms.

- The results of this study may help physicians to pay attention on vulvovaginal atrophy and its consequences in this group of HIV positive women.

Limitations:

- It's a cross-sectional design study
- There were some differences in the clinical characteristics of the HIV-positive and HIV-negative women.

Introduction

Dyspareunia is defined as persistent or recurrent genital pain that occurs just before, during or after intercourse. It is one of the most common problems reported by menopausal women. The variation in the frequency of dyspareunia probably reflects many issues including sociocultural aspects, the period of observation during which the condition was evaluated (ever, the past year) and the duration or design of the study under discussion (questionnaire wording, participants). [1]

For women of all ages, the pain caused by dyspareunia often results in distress, impaired sexual functioning and poor sexual enjoyment, difficulty in relationships and a poorer quality of life. In postmenopausal women, dyspareunia may also intensify personal issues related to aging, body image and health. [2]

As with most of the sexual difficulties faced by women at midlife and beyond, dyspareunia is typically considered a consequence of declining ovarian hormone levels and is usually attributed to vaginal atrophy; [3] however, other

factors may also be involved. [4] In fact, psychosexual and biological factors (including muscular, endocrine, immune, neurological, vascular and iatrogenic factors) that predispose to, precipitate and perpetuate the condition may interact to different degrees in the individual woman, contributing to a continuum of symptoms of increasing severity, with the potential to impair sexual intercourse[5,5]. Age, [6] depression, ~~nervousness~~ anxiety and sexual dysfunction in the partner [4,5] are some other factors associated with dyspareunia. It seems that cognitive-emotional variables (catastrophization, depression, anxiety) are significant predictors of dyspareunia and relationship adjustment variables were inversely associated with pain severity.[7] Findings also suggest that dyspareunia impacts not only the psychosexual adjustment of affected women but also that of their partners.[8]

Menopausal women who are HIV-positive may present a unique set of issues that could affect their sexuality. These issues may include the meaning of their illness, their quality of life, HIV transmissibility, and the dilemma of whether or not to disclose the condition to their partner. Florence et al. reported sexual dysfunction to be common in HIV-positive women, principally as a result of their HIV status and of psychological factors that included depression, irritability and anxiety. [7-9] On the other hand, women with better mental health after HIV diagnosis, a more positive attitude towards living with HIV, a better quality of life, fewer HIV-related symptoms and who had never used injectable drugs were found to have better sexual functioning. [8-10] A possible role of antiretroviral drugs in causing sexual dysfunction has been a matter of debate. Whereas some studies have suggested that antiretroviral therapy indeed plays a role in sexual function, others have failed to find any such association. [9,11]

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The majority of studies on dyspareunia have failed to deal with factors associated with the HIV infection, a topic yet to be fully investigated in HIV-positive women during the aging process. Therefore, the objectives of the present study were to evaluate whether dyspareunia is associated with HIV status in middle-aged women and to assess the factors associated with dyspareunia in HIV-positive middle-aged women.

Methods

Study design

A cross-sectional study was conducted in which 537 women of 40 to 60 years of age, 273 of whom were HIV-positive and 264 HIV-negative~~,~~ were screened for inclusion. Patients were recruited ~~These women were receiving care~~ at the infectious diseases and HIV outpatient clinics (HIV positive women) and at the menopausal ambulatory care (HIV negative women), both at the Teaching Hospital of the University of Campinas (UNICAMP)~~, at the genital infections and the menopausal outpatient clinics of CAISM/UNICAMP, and~~ Patients were also invited to participate at the infectious diseases outpatient public clinic (HIV positive women)~~of the Eduardo de Menezes Hospital~~ in Belo Horizonte ~~were invited to participate in the study.~~ Of these, 178 HIV- negative women and 128 HIV- positive women had had vaginal intercourse in the previous month and were willing to answer a questionnaire on dyspareunia. These women were then admitted to the study.

For inclusion in the HIV-positive group, laboratory confirmation~~, through blood samples collected at the moment of admission in the present study,~~ of the

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women's seropositive status by one of the recommended tests (ELISA or Western Blot) was required (all of them had it), while the women recruited to the HIV-negative group had to have tested negative. The blood samples tests of HIV negative and positive women were collected at the moment of admission in the present study (FSH, LH and TSH for all, ELISA or Western Blot HIV tests for HIV negative women and Viral load and CD4 cells for HIV positive women . Exclusion criteria consisted of nursing mothers, bilaterally oophorectomized women and those unable to answer the questionnaire.

The evaluation instrument was ~~based on~~ the Short Personal Experiences Questionnaire (SPEQ). [~~10,11~~12,13] Sociodemographic, clinical, behavioral and reproductive characteristics were assessed as well as issues relating to the HIV infection and partner-related factors.

~~Blood samples were collected at the moment of admission in the present study, and the rapid test was carried out and compared with the gold standard (ELISA and Western blot).~~

~~***Sample size***~~

~~Sample size was calculated by estimating the prevalence of sexual dysfunction in HIV-negative menopausal women at 35.9%~~ [12] ~~and the prevalence of sexual dysfunction in HIV-positive women at 60.0%.~~ [13] ~~To enable comparisons to be drawn between the HIV-positive and HIV-negative groups, the number of women required was calculated at 74 per group for an alpha error of 0.05 and a beta error of 0.20; however, to enable analysis to be made of the HIV-positive group alone, the required number was 188 women (with a difference of 7 percentage points). Since the actual sample size achieved was 128, the absolute difference was 8.5%.~~

Dependent variable

The dependent variable dyspareunia, defined as pain during sexual intercourse, was graded from 1 to 6, where 1 referred to the absence of pain and 6 to maximum pain. A score of less than 2 was considered to represent the absence of dyspareunia and a score of 2 or more to represent the presence of dyspareunia. [12,13,14] ~~Dyspareunia was defined as pain during sexual intercourse in accordance with a pain intensity score of 2 or more within a scale of 1 to 6.~~

Independent variables

The independent variables were dichotomized as follows: HIV status (positive / negative); skin color (white / other); marital status (has a stable partner/ no stable partner); schooling (≤ 7 years / ≥ 8 years); employment (yes: / no); monthly family income (≤ USD750 / > USD750); receives pension (yes / no); smokes (yes / never or past smoker); alcohol use (currently drinks or used to drink / never drank); hot flushes (yes / no); depression (yes / no); vaginal dryness (yes / no); urinary incontinence (yes / no); weight gain (yes / no); muscle and joint pain (yes / no); self-perception of health (excellent or good / poor or very poor); suffers or has already suffered some form of physical or emotional violence (yes / no); has been forced to have intercourse (yes / no); uses statins (yes / no); chronic disease: hypothyroidism (yes / no); FSH (<40/≥40), LH (<25.7 / ≥ 25.7); age at first sexual intercourse (≤ 19 years / ≥ 20 years); other type of sexual intercourse in the preceding month: ~~active~~ giving oral sex (yes / no); ~~passive~~ receiving oral sex (yes / no); woman lives with

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sexual partner (yes / no); ~~menopausal status: (pre- or perimenopausal/ menopausal)~~; number of sexual partners in the previous year (none / ≥ 1); partner underwent HIV testing (yes / no); quality of life following diagnosis (changed / unchanged); CD4 cell count (<350 / ≥ 350); CD4 cell count nadir (<199; ≥ 200); use of antiretroviral drug 3TC (Lamivudine, Epivir) (yes/ no); use of antiretroviral drug Tenofovir (yes / no); use of antiretroviral drug lamivudine/zidovudine (yes / no); use of antiretroviral drug Efavirenz (yes / no); antiretroviral drug used in the past: lamivudine/zidovudine (yes / no); antiretroviral drug used in the past: Efavirenz (yes/ no). Menopausal status was classified as premenopausal, perimenopausal or postmenopausal. Women were considered premenopausal if they continued to have regular menstrual cycles similar to those present during the woman's reproductive life. They were considered to be in the perimenopause if their menstrual cycles were irregular and they had been amenorrheic for less than 12 months. Finally, women were classified as postmenopausal if they had been amenorrheic for 12 months or more.[15] Data on physical activity was obtained through two questions: Do you practice physical exercise or participate in sports every week? How often in a week do you practice physical exercise or participate in sports?. It was classified in up two times a week or 3 or more times a week. Vaginal lubrication during sexual activity was graded from 1 to 6, where 1 referred to the absence of lubrication and 6 to maximum lubrication. This was dichotomized into 4 or less

or more than 4.

Statistical analysis

A bivariate analysis was performed in which dyspareunia was considered the dependent variable (dyspareunia) and analyzed as a function of the independent variables. Pearson's chi square test and the Yates correction were used to compare the groups. [14-16] The Poisson multiple regression analysis [15-17] was adjusted in the various models for each one of the independent variables to evaluate the factors associated with the presence of dyspareunia.

Ethics

The study was approved by the internal review board of CAISM/UNICAMP and was conducted in compliance with the current version of the Declaration of Helsinki and with Resolution 196/96 of the Brazilian National Committee for Ethics in Research (CONEP) and its subsequent revisions. This study forms part of a larger study evaluating menopausal symptoms, bone mass, sexual function and metabolic markers. Process: CEP: 407/2010, CAAE 0313.0.146.000-10.

Women who agreed to participate in the study after receiving instructions from the researchers and who signed a free informed consent form were included.

Results

The HIV-positive women were younger and less likely to have a steady partner, to be employed or to have a formal education compared to the HIV-negative women. More than half the HIV-positive women were pre- or perimenopausal. The characteristics of the women interviewed are shown in Table 1.

Overall, 41.4% (n=53) of the HIV-positive women and 34.8% (n=62) of the HIV-negative women reported dyspareunia. There was no association between HIV status and dyspareunia (p=0.242) ~~(data not shown as table)~~. Furthermore, in the multiple regression analysis of the entire sample of HIV-positive and HIV-negative women taken together (n=306), dyspareunia was not associated with HIV status, but was associated with vaginal dryness (PR=2.06, 95%CI: 1.37-3.10, p=0.001) and urinary incontinence (PR=1.68, 95%CI: 1.14-2.46, p=0.008). ~~Predictive variables considered: HIV status (positive / negative); skin color (white / other); marital status (has a stable partner/ no stable partner); schooling (≤ 7 years / ≥ 8 years); employment (yes: / no); monthly family income (≤ R$1.500 / > R$1500); receives pension (yes / no); smokes (yes / never or past smoker); alcohol use (currently drinks or used to drink / never drank); hot flushes (yes / no); depression (yes / no); vaginal dryness (yes / no); urinary incontinence (yes / no); weight gain (yes / no); muscle and joint pain (yes / no); self-perception of health (excellent or good / poor or very poor); suffers or has already suffered some form of physical or emotional violence (yes / no); has been forced to have intercourse (yes / no); uses statins (yes / no); chronic disease: hypothyroidism (yes / no); LH (<25.7 / ≥ 25.7); age at first sexual intercourse (≤ 19 years / ≥ 20 years); other type of sexual intercourse in the preceding month: active oral sex (yes / no); passive oral sex (yes / no); woman lives~~

~~with sexual partner (yes / no); menopausal status: (pre- or perimenopausal/ menopausal); number of sexual partners in the previous year (none / ≥ 1).~~

~~(Table not presented).~~

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In the HIV-positive group, 91.4% of the women were currently in use of antiretroviral therapy (ART) and, of these, 87% reported using ART regularly (data not presented as table). Approximately 77% of the HIV-positive women had a CD4 cell count nadir >200. The most common way in which HIV had been acquired was by heterosexual transmission, and the average duration of the HIV infection was 9.5 ± 5.6 years (mean ± SD), with a mean duration of therapy of 8.7 years ±4.5 (mean ± SD). A more detailed description of the HIV-infected women is provided in Table 2.

Bivariate analysis revealed an association between dyspareunia in the HIV-positive women and having a steady partner (p=0.047); the woman's partner having undergone HIV testing (p=0.020); vaginal dryness (p<0.001); muscle/joint pain (p=0.021); physical/emotional violence (p=0.049); urinary incontinence (p=0.004); and the use of lamivudine/zidovudine (p=0.048), Table 3.

According to the Poisson multiple regression analysis, the principal factors associated with dyspareunia in the group of HIV-positive women were: vaginal dryness (PR = 1.96; 95%CI: 1.10- 3.50; p=0.023) and urinary incontinence (PR=1.86; 95%CI: 1.06-3.27; p = 0.031) (Table 4).

Discussion

The objectives of this study were to evaluate whether HIV status was associated with dyspareunia and to assess the factors associated with pain during sexual intercourse in HIV-positive women of 40 to 60 years of age. The calculated number of women required for the sample size was at 74 per group[14]; however, to enable analysis of the HIV-positive group alone, the required number was 188 women[18]. Since the actual sample size achieved was 128, the absolute difference was 8.5%, acceptable since it is less than 10%. Information on dyspareunia in HIV positive women is scarce, especially in middle-aged women. To the best of our knowledge, no other studies have been conducted on dyspareunia in HIV-positive women ~~of 40 to 60 years of age~~. It has been reported that sexual function in HIV-positive women may be driven principally by psychological factors and ~~by~~other-problems ~~originated by~~related to HIV ~~status~~infection. ~~13,16~~[18,19] The present study, however, found that in the overall sample of HIV-positive and negative women dyspareunia was not affected by HIV status. This finding is in agreement with the results of another author, who also reported that few women believed HIV in itself to be the cause of any decline in their sexual functioning, since those women had good immunovirological status ~~few HIV-related symptoms~~. ~~8~~[8,10] One supposes that results would be different in a sample of women without a good ~~many~~ HIV ~~symptoms~~control. In the present study, more than three-quarters of the HIV-positive patients had a CD4 cell count nadir > 200 and CD4 cell counts > 500 in their last evaluation, thus reflecting adequate control of the disease. This may partially explain why no association was found between HIV status and dyspareunia. In line with this, another study showed that women with CD4 counts ≤199 cells/μL reported poorer sexual functioning compared to those

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whose cell count was ≥ 200. [17][20] Other studies have shown that CD4 cell count nadir may also have long-term consequences in terms of prognosis and mortality. [18][21]

Nevertheless, the CD4 cell count nadir and the last CD4 evaluation were not associated with dyspareunia in the present study, probably because of the small number of women with these low values.

The most important factors associated with dyspareunia in the logistic regression analysis, in HIV positive and negative groups analyzed together and in the HIV group analysis were vaginal dryness and urinary incontinence, both of which are urogenital disorders associated with estrogen deficiency. The association between vaginal dryness and pain during sexual intercourse has been well documented in the literature, in addition to its consequence on vulvovaginal health. [19,20][22,23,24] With respect to the association between urinary incontinence and dyspareunia, the findings of the present study are in agreement with the results published by Salonia et al., evaluated 216 women with urinary incontinence and found 44% of dyspareunia in these women. ~~who compared 216 women with urinary incontinence to healthy women without any urinary symptoms and found 44% of dyspareunia in women with urinary incontinence.~~ [21][25] The type of urinary incontinence was not evaluated in the present study. Nevertheless, there is good evidence that the effects of urinary incontinence on sexual functioning are similar irrespective of whether the condition has been classified as stress, urge, mixed incontinence[22][26] or even interstitial cystitis[27] Urinary incontinence ~~leads to~~ is associated with feelings of embarrassment and inadequacy as well as low self-esteem. It may also be associated to dyspareunia. [22][25]

Factors associated with dyspareunia in HIV positive women:

In the present study, more than three-quarters of the HIV-positive patients had a CD4 cell count nadir > 200 and CD4 cell counts > 500 in their last evaluation, reflecting adequate control of the disease. This may partially explain why no association was found between HIV status and dyspareunia. In line with this, another study showed that women with CD4 counts ≤199 cells/μL reported poorer sexual functioning compared to those whose cell count was ≥ 200.[17] Other studies have shown that CD4 cell count nadir may also have long-term consequences in terms of prognosis and mortality.[18]

Nevertheless, the CD4 cell count nadir and the last CD4 evaluation were not associated with dyspareunia in the present study, probably because of the small number of women with these low values.

The most important factors associated with dyspareunia in the logistic regression analysis, in HIV positive and negative groups, were vaginal dryness and urinary incontinence, both of which are urogenital disorders associated with estrogen deficiency. The association between vaginal dryness and pain during sexual intercourse has been well documented in the literature.[19,20] With respect to the association between urinary incontinence and dyspareunia, the findings of the present study are in agreement with the results published by Salonia et al., who compared 216 women with urinary incontinence to healthy women without any urinary symptoms and found 44% of dyspareunia in women with urinary incontinence.[21] The type of urinary incontinence was not evaluated in the present study. Nevertheless, there is good evidence that the effects of urinary incontinence on sexual functioning are similar irrespective of

~~whether the condition has been classified as stress, urge or mixed incontinence. Urinary incontinence leads to feelings of embarrassment and inadequacy as well as low self-esteem. It may also lead to dyspareunia.~~ [22]

In the bivariate analysis, the fact that the woman's partner had not been tested for HIV was associated with less dyspareunia. It is reasonable to speculate that not knowing her partner's HIV status may in some way "minimize" a woman's concerns regarding transmission and reduce the probability of tension and dyspareunia. [23–28] Another factor related to the sexual partner that was associated with an increase in dyspareunia in the bivariate analysis was the woman having a steady partner, although this association was borderline,. One explanation for this finding may lie in the psychological problems generated by the infection itself, which may arise more frequently in stable relationships. [23,24,28,29] As one has not controlled for frequency of intercourse, one thought is dyspareunia due a lower frequency of intercourse rather than quality of the relationship.

Results of the bivariate analysis revealed an association between physical/emotional violence and dyspareunia. Violence is known to be associated with poorer psychological adjustment and adverse sexual health outcomes in women. [25,26,30,31] In addition, having muscle pain was associated with dyspareunia in the bivariate analysis. This finding is in line with another study showing that musculoskeletal pain often interferes with sex and may be associated with dyspareunia. [27–32] A borderline association was found between the use of lamivudine/zidovudine and dyspareunia; however, no explanation for this association was found in the literature. One may hypothesize that

dyspareunia in these women could be due depression side effects of these drugs.

Some limitations to the present study must be taken into account. First, its cross-sectional design does not permit any conclusions to be drawn with respect to causality. It is also important to note that it was a clinical sample. So, the results found in the present study may not be extrapolated to the general population. Furthermore, there were some differences in the clinical characteristics of the HIV-positive and HIV-negative women. These differences could be attributed to the fact that the HIV-negative women were selected at specialist outpatient clinics providing care to menopausal women. By selecting HIV positive women also in menopausal outpatient care, maybe groups would be similar. Nevertheless, multivariate analysis, conducted in a sufficiently large sample of women after controlling for confounding factors, confirmed that HIV infection was not significantly associated with dyspareunia. Good control of the HIV infection and the regular use of antiretroviral therapy by the majority of the women may have brought this group of women closer to the HIV-negative group in terms of their characteristics.

Conclusions

In this study population, HIV infection was not associated with the presence of dyspareunia. The principal factors associated with dyspareunia in HIV-positive women were vaginal dryness and urinary incontinence. These data indicate a need for multidisciplinary care for HIV-positive menopausal women, paying

particular attention to ensuring the women's compliance with antiretroviral therapy and offering improved care when these two clinical situations are present to ensure that these women come as close as possible in this respect to HIV-negative women. Greater attention to dyspareunia as a potential component of women's general HIV and sexual care is warranted. A proactive approach to conversations about vulvovaginal atrophy would improve management of dyspareunia and vaginal dryness. In addition to improving the quality of these women's sexual life, we hypothesize that appropriate management of this issue may reduce the likelihood of lesions on the vaginal wall, which may act as a portal of entry for other infections.

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Competing Interest: None declared.

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Competing interests: None declared

As corresponding author, I confirm that I have collected ICMJE Uniform Disclosure Forms for Potential Conflicts of Interest from every author and no Conflicts of Interest exist for any of the authors.

Data sharing

We confirm that is no additional unpublished data from the present study available.

Extra data

The instrument used to collect data is available by emailing anarvaladares@gmail.com

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Table 1– Some characteristics of women according to HIV status

Characteristic	Group HIV-infected (%) (n=128)	HIV-uninfected (%) (n=178)	*p* Value
Age (years)			
40 – 44	43.8	24.7	<0.002[1]
45 – 49	28.9	29.2	
50 – 54	15.6	23.1	
≥ 55	11.7	23,0	
Skin color			
White	35.2	47.2	0.047[2]
Non-White	64.8	52.8	

Number of deliveries			
Up to 1	25.0	25.4	>0.999[2]
≥2	75.0	74.6	
Marital status			
With partner	58.6	87.1	<0.001 [2]
Without partner	41.4	12.9	
Schooling (years)			
≤7	62.5	40,4	<0.002[1]
8-11	23.4	37,1	
≥12	14.1	22,5	
Employment status			
Yes	59.4	71.9	0.030[2]
No	40.6	28.1	
Menopausal status			
Premenopausal	39.8	24.7	<0.002 [1]
Perimenopausal	28.1	21.4	
Postmenopausal	32.1	53.9	
Current smoking t			
Yes/ Former	28,1	15.2	0.009 [2]
No	71,9	84.8	
Physical activity			
Up to 2 times/week	77.3	74.2	0.614[2]
>3 times/week	22.7	25.8	

[1]Pearson's Chi-square; & Yates's Chi-square

Table 1– Characteristics of women according to HIV status

Characteristic	Group HIV-infected (%) (n=128)	HIV-uninfected (%) (n=178)	*p* Value
Age (years)			
40 – 44	43.8	24.7	<0,002 #
45 – 49	28.9	29.2	
50 – 54	15.6	23.1	
≥ 55	11.7	23,0	
Race/ethnicity			
White	35.2	47.2	0,047 &
Non-White	64.8	52.8	
Number of deliveries			
Up to 1	25.0	25.4	>0.999 &
≥2	75.0	74.6	
Marital status			
With partner	58.6	87.1	<0,001 &
Without partner	41.4	12.9	
Schooling (years)			
≤7	62.5	40,4	<0,002 #
8-11	23.4	37,1	
≥12	14.1	22,5	
Employment status			
Yes	59.4	71.9	0.030 &
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Menopausal status			
Premenopausal	39.8	24.7	<0,002 #
Perimenopausal	28.1	21.4	
Postmenopausal	32.1	53.9	
Smoking habit			
Yes/ Former	28,1	15.2	0,009 &
No	71,9	84.8	
Physical activity			
Up to 2 times/week	77.3	74.2	0,614 &
>3 times/week	22.7	25.8	

* Sample of women with partner and information on occurrence or not of dispareunia in the last month

Pearson's Chi-square; & Yates's Chi-square

Table 2 – Characteristics associated to HIV status associated with dyspareunia in women with sexual partner in the month before the interview (n=128)

Characteristics	N	%
HIV duration of infection (n=125) (years)	Mean: 9.5	SD: 5.06
Duration of HIV therapy (n=93) (years)	Mean: 8.7	SD: 4.47
Nadir CD4 levels (a)		
0 – 100	18	14.5

101 – 200	10	8.1
201 – 500	62	50.0
> 500	34	27.4
Last CD4 levels (a)		
0 – 100	5	4.0
101 – 200	1	0.8
201 – 500	43	34.7
> 500	75	60.5
Total	**124**	**100.0**
HIV risk factor for acquisition		
heterosexual acquisition	97	75.8
Illicit drug use	3	2.3
blood transfusion	2	1.6
	26	20.3
Total	**128**	**100.0**
Use of TARV		
Yes	117	91.4
No	11	8.6
Total	**128**	**100.0**

(a) Missing information

Table 2 – Characteristics associated to HIV status associated with dyspareunia in women with sexual partner in the month before the interview (n=128)

Characteristics	N	%
Nadir CD4 levels (a)		
0 – 100	18	14.5
101 – 200	10	8.1
201 – 500	62	50.0
> 500	34	27.4
Last CD4 levels (a)		
0 – 100	5	4.0
101 – 200	1	0.8

201 – 500	43	34.7
> 500	75	60.5
Total	**124**	**100.0**
HIV risk factor for acquisition		
heterosexual *acquisition*	97	75.8
Illicit drug use	3	2.3
blood transfusion	2	1.6
Não sabe/ Não respondeu	26	20.3
Total	**128**	**100.0**
Use of TARV		
Yes	117	91.4
No	11	8.6
Total	**128**	**100.0**
HIV duration of infection (n=125) (years)	Mean: 9.5	SD: 5.06
Duration of HIV therapy (n=93)	Mean: 8.7	SD: 4.47

(years)

(a) Missing information

Table 3 – Factors associated with dyspareunia (score >2) in middle-aged HIV positive women: bivariate analysis

Variable	n	Dyspareunia% Score>2	Score<2	p
Marital status				**0.047**
Married/live together	75	49.3	50.7	
Don´t live together	53	30.2	69.8	
Did partner have HIV test?				**0.020**
Yes	88	50.0	50.0	
No	27	22.2	77.8	
Vaginal dryness				**<0.001**
Yes	53	58.5	41.5	
No	71	26.8	73.2	
Muscular / articular pain				**0.021**
Yes	83	49.4	50.6	
No	45	26.7	73.3	
Physical/ Emotional violence				**0.049**
Yes	128	55.5	44.5	
No	174	32.8	67.2	

Urinary Incontinence				**0.004**
Yes	41	61.0	39.0	
No	87	32.2	67.8	
Use of biovir				**0.048**
Yes	57	29.8	70.2	
No	63	49.2	50.8	

Table 3 – Factors associated with dyspareunia (score >2) in middle-aged HIV positive women: bivariate analysis

		Dyspareunia%		
Variable	N	Score>2	Score<2	p *
Marital status				**0.047**
Married/live together	75	49.3	50.7	
Don´t live together	53	30.2	69.8	
Did partner have HIV test?				**0.020**
Yes	88	50.0	50.0	
No	27	22.2	77.8	
Vaginal dryness				**<0.001**
Yes	53	58.5	41.5	

No	71	26.8	73.2	
Muscular / articular pain				**0.021**
Yes	83	49.4	50.6	
No	45	26.7	73.3	
Physical/ Emotional violence				**0,049**
Yes	128	55.5	44.5	
No	174	32.8	67.2	
Urinary Incontinence				**0,004**
Yes	41	61.0	39.0	
No	87	32.2	67.8	
Use of biovir				**0.048**
Yes	57	29.8	70.2	
No	63	49.2	50.8	

Predictive variables considered: skin color (white / other); marital status (has a stable partner/ no stable partner); schooling (≤ 7 years / ≥ 8 years); employment (yes: / no); monthly family income (≤ R$1.500 / > R$1500); receives pension (yes / no); smokes (yes /

never or past smoker); alcohol use (currently drinks or used to drink / never drank); hot flushes (yes / no); depression (yes / no); vaginal dryness (yes / no); urinary incontinence (yes / no); weight gain (yes / no); muscle and joint pain (yes / no); self-perception of health (excellent or good / poor or very poor); suffers or has already suffered some form of physical or emotional violence (yes / no); has been forced to have intercourse (yes / no); uses statins (yes / no); chronic disease: hypothyroidism (yes / no); LH (<25.7 / ≥ 25.7); age at first sexual intercourse (≤ 19 years / ≥ 20 years); other type of sexual intercourse in the preceding month: active oral sex (yes / no); passive oral sex (yes / no); woman lives with sexual partner (yes / no); menopausal status: (pre- or perimenopausal/ menopausal); number of sexual partners in the previous year (none / ≥ 1); partner underwent HIV testing (yes / no); quality of life following diagnosis (changed / unchanged); CD4 cell count (<350 / ≥ 350); CD4 cell count nadir (<199; ≥ 200); use of antiretroviral drug 3TC (Lamivudine, Epivir) (yes/ no); use of antiretroviral drug Tenofovir (yes / no); use of antiretroviral drug Lamivudine/zidovudine (yes / no); use of antiretroviral drug Efavirenz (yes / no); antiretroviral drug used in the past: Lamivudine/zidovudine (yes / no); antiretroviral drug used in the past: Efavirenz (yes/ no).

Table 4 – Variables associated with dyspareunia in HIV positive women with sexual partner in the month before the interview. Poisson multiple regression [n=124]

Variable	PR	95%CI	p-value
Vaginal dryness	1.96	1.10 – 3.50	**0.023**
Urinary incontinence	1.86	1.06 – 3.27	**0.031**

PR: prevalence ratio; CI 95%: 95% confidence interval; p: p-value

~~**Tabela 4** – Variables associated with dyspareunia in HIV positive women with sexual partner in the month before the interview. Poisson multiple regression [n=124]~~

~~Variable~~	~~PR~~	~~95%CI~~	~~p-value~~

Vaginal dryness	1.96	1.10 – 3.50	**0.023**
Urinary incontinence	1.86	1.06 – 3.27	**0.031**

PR: prevalence ratio; CI 95%: 95% confidence interval; p: p-value

Predictive variables considered: skin color (white / other); marital status (has a stable partner/ no stable partner); schooling (≤ 7 years / ≥ 8 years); employment (yes: / no); monthly family income (≤ R$1.500 / > R$1500); receives pension (yes / no); smokes (yes / never or past smoker); alcohol use (currently drinks or used to drink / never drank); hot flushes (yes / no); depression (yes / no); vaginal dryness (yes / no); urinary incontinence (yes / no); weight gain (yes / no); muscle and joint pain (yes / no); self-perception of health (excellent or good / poor or very poor); suffers or has already suffered some form of physical or emotional violence (yes / no); has been forced to have intercourse (yes / no); uses statins (yes / no); chronic disease: hypothyroidism (yes / no); LH (<25.7 / ≥ 25.7); age at first sexual intercourse (≤ 19 years / ≥ 20 years); other type of sexual intercourse in the preceding month: active oral sex (yes / no); passive oral sex (yes / no); woman lives with sexual partner (yes / no); menopausal status: (pre- or perimenopausal/ menopausal); number of sexual partners in the previous year (none / ≥ 1); partner underwent HIV testing (yes / no); quality of life following diagnosis (changed / unchanged); CD4 cell count (<350 / ≥ 350); CD4 cell count nadir (<199; ≥ 200); use of antiretroviral drug 3TC (Lamivudine, Epivir) (yes/ no); use of antiretroviral drug Tenofovir (yes / no); use of antiretroviral drug Lamivudine/zidovudine (yes / no); use of antiretroviral drug Efavirenz (yes / no); antiretroviral drug used in the past: Lamivudine/zidovudine (yes / no); antiretroviral drug used in the past: Efavirenz (yes/ no).

checklist **Dyspareunia in HIV positive and negative middle-aged women**

	Item No	Recommendation
okTitle and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found
Introduction		
Ok background/rationale	2	Explain the scientific background and rationale for the investigation being reported
Ok Objectives	3	State specific objectives, including any prespecified hypotheses
Methods		
Ok Study design	4	Present key elements of study design early in the paper
Ok Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection
Ok Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case
Ok Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
Ok Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group
Ok Bias	9	Describe any efforts to address potential sources of bias
Ok Study size	10	Explain how the study size was arrived at
Ok Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
Ok Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding
		(*b*) Describe any methods used to examine subgroups and interactions
		(*c*) Explain how missing data were addressed
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy
		(*e*) Describe any sensitivity analyses

Continued on next page

Results		
Ok Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed
		(b) Give reasons for non-participation at each stage
		(c) Consider use of a flow diagram
Ok Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders
		(b) Indicate number of participants with missing data for each variable of interest
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)
Ok Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time
		Case-control study—Report numbers in each exposure category, or summary measures of exposure
		Cross-sectional study—Report numbers of outcome events or summary measures
Ok Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included
		(*b*) Report category boundaries when continuous variables were categorized
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Ok Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses
Discussion		
Ok Key results	18	Summarise key results with reference to study objectives
Ok Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias
Ok Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
Ok Generalisability	21	Discuss the generalisability (external validity) of the study results
Other information		
Ok Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.