PHARMACOTHERAPY

# Sexual Dysfunctions Among People Living With HIV With Long-Term Treatment With Antiretroviral Therapy

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## ABSTRACT

**Introduction:** Sexuality plays an essential role in the psychosocial well-being of people living with HIV (PLHIV) but it is still less assessed by healthcare professionals during treatment.

**Aim:** To investigate the frequency of those screening positive for sexual dysfunction (SD) and associated factors according to gender/sexual orientation in PLHIV under long-term treatment with antiretroviral therapy (ART).

**Methods:** Between September 2013 and October 2016, 234 PLHIV adults in treatment in São Paulo were included. Participants were sexually active, did not present sexual orientation disorder or body dysmorphic disorder, and did not use sexual hormones. We performed clinical interviews and measured levels of depression, anxiety, and levels of sexual hormones. SD was assessed using a self-report questionnaire.

**Main Outcome Measures:** Proportion of participants screening positive for SD in the International Index of Erectile Function, the Index of Premature Ejaculation, and the Female Sexual Function Index. In the regression analyses, the outcome SD considered any SD presented with disregard to gender.

**Results:** 70% of participants reported consistent adherence to ART and 96% had an undetectable viral load. The median (Md) duration of ART was 198 months (inter quartil range, IQR 111.6−230.4) and the median CD4 was 655 cells/mm$^3$ (IQR 443−871). Screening positive for erectile dysfunction was 49.7%, premature ejaculation 16.9%, female sexual dysfunction 27.4% and hypoactive desire 45.1%. Lower testosterone and prolactin levels were associated with erectile dysfunction in heterosexual men ($n$ = 58); lower levels of oestradiol and higher levels of follicle stimulating hormone were associated with female sexual dysfunction and hypoactive desire in female participants ($n$ = 63). The multivariable model used included comorbidities and hormonal abnormality and found that age (odds ratio, OR = 1.04, 95% confidence interval, 95%CI 1.00−1.08, $P$ = .026) and the presence of depression/anxiety (OR = 2.96; 95%CI 1.52−5.77; $P$ = .001) were associated with SD. Also, men reporting engaging in sex with other men were associated with screening positive for SD (OR 2.66; 95%CI 1.52−5.77, $P$ = .013).

During treatment of PLHIV, it is important to evaluate sexual health and symptoms of depression and anxiety specifically.

The strength of this study consists in evaluating PLHIV who have been in long-term treatment with ART and analyzing those screening positive for SD and associated factors for each group (heterosexual men, men reporting engaging in sex with other men, and women). Limitation includes the difficulty to generalize the findings of the study, and not exploring women's sexual orientation.

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**Conclusion:** PLHIV in long-term treatment with ART presented alarming rates of depression/anxiety which in turn is correlated with sexual and physical health problems. **Scanavino MDT, Mori E, Nisida VV, et al. Sexual Dysfunctions Among People Living With HIV With Long-Term Treatment With Antiretroviral Therapy. Sex Med 2022;10:100542.**



**Key Words:** Sexual dysfunction; HIV; Mental health; Erectile dysfunction; Hypoactive desire

## INTRODUCTION

Sexuality plays an essential role in the psychosocial well-being of people living with HIV (PLHIV). Furthermore, it is a crucial factor in its epidemiology and transmission. However, sexual functioning is scarcely assessed by healthcare professionals during the treatment of PLHIV.[1−3] Despite several studies that evaluate risk factors and sexual dysfunction (SD) in PLHIV, only a few collected data from heterosexual men, men reporting engaging in sex with other men (MSM), and women in the same study, hindering the comparison of sexual functions among the 3 groups. Several factors have shown to be associated with SD among PLHIV, including psychological and hormonal factors, comorbidities, and the use of medications. However, the pathogenesis of SD is complex and multifactorial, and many issues remain unclear.[1,4]

The introduction of combined antiretroviral therapy (ART) in the mid-1990s improved the life expectancy of PLHIV. In parallel, though, higher life expectancy has also increased HIV-related comorbidities, such as endocrine and metabolic diseases (the most common ones), and SD.

SD impacts the quality of life and often leads to individuals adopting harmful behaviors, such as low adherence to ART and engagement in unprotected sex.[1]

The sexual health of women living with HIV is often overlooked by clinicians in clinical practice, besides its high prevalence. One study found that 89.2% of women living with HIV had female sexual dysfunction (FSD).[5] Many factors can affect female sexual function, such as psychological, socio-cultural, and couple relationship factors.[6]

Among men living with HIV under ART, the previously reported prevalence of erectile dysfunction (ED) ranges from 9 to 74%.[2] Such a discrepancy might be due to methodological differences among studies, their design, sample size, and different comorbidities. Among MSM who were submitted to an anonymous self-report questionnaire, 31% declared that they reached orgasm too quickly, 24% too slowly, and 19% could not reach orgasm at all.[7] Decreased erectile function, decreased satisfaction, and decreased desire were found to be more prevalent in MSM HIV infected than non-infected.[8,9]

Although several studies have assessed the prevalence of SD in PLHIV, just a few studies specifically address this outcome among individuals under long-term exposure to ART.[10]

As far as ART duration is concerned, one study found a prevalence of 52.2% of moderate/severe SD among men with a total duration of ART over 81 months. In contrast, the prevalence of ED among men using ART for less than 43 months was 30.7%.[11] Even though the role of ART in the pathogenesis of ED is still controversial, the duration of treatment was found to be associated with ED.[11] Nevertheless, how the occurrence of erectile dysfunction is affected by the duration of ART needs to be further investigated.[11−13]

We estimated the frequency of screening positive for SD on self-report measures and associated factors, according to gender and sexual orientation categories, namely, heterosexual men, MSM, and women.

Due to the lack of studies investigating well-being and sexuality in PLHIV under long-term treatment with ART, we decided to investigate the prevalence of SD and associated factors in this specific population.

Based on former studies we hypothesized the proportion of PLHIV under long-term treatment with ART would present frequencies of screening positive for SD on self-report measures greater than 20%; and that a different pattern of associated factors to SD would appear, according to gender and sexual orientation categories. Finally, we hypothesized that some relevant factors would be associated with SD considering the whole sample of PLHIV.

## MATERIALS AND METHODS

### Participants and Procedures

A cross-sectional, observational study was carried out at [masked for review], a highly regarded HIV outpatient care center. Patients were recruited in their routine medical follow-up, from September 2013 to October 2016. Enrolled participants were 18 years old or over and literate. We excluded individuals diagnosed with sexual orientation disorder (International Statistical Classification of Diseases and Related Health Problems - ICD-10 F64) or body dysmorphic disorder (ICD-10 F45.2), in addition to those who reported no sexual activity in the previous month by choice, took sexual hormones in the previous 6 months, reported SD before the diagnosis of HIV, and sex workers. Participants gave written consent to be part of this

study. They completed a 1-hour questionnaire that encompassed a sociodemographic interview, a clinical and psychiatric evaluation, and SD assessment through a self-response platform on RedCap (a web-based application developed by Vanderbilt University, Nashville, TN, USA) hosted at [masked for review]. Routine laboratory assessment of HIV parameters (CD4 counts and HIV viral loads) and hormonal blood tests (testosterone, sex hormone-binding globulin, follicle-stimulating hormone, oestradiol, prolactin, progesterone) were performed. The study protocol was reviewed and approved by the ethics committee of [masked for review].

## Measures

Participants reported their age, gender, legal marital status, race, educational background, employment, family monthly income, sexual orientation, and HIV serostatus.

## Psychopathology Measures

Mini-International Neuropsychiatric Interview (MINI) is a short standardized diagnostic interview compatible with the Structured Clinical Interview for DSM-III-R, Patient Version (SCID-P), and reliability indices were found to be satisfactory (Kappa > .60). MINI was validated in the Brazilian context.[14] This interview was used to assess alcohol and drug abuse and addiction.

The Portuguese version of the Beck Anxiety Inventory (BAI) was validated for use in Brazil and is reliable (Cronbach's alpha = 0.76). The Beck Depression Inventory II (BDI) Portuguese version was validated for Brazil (Cronbach's alpha = 0.93).[15] Both BAI and BDI are composed of a 21-item self-reported scale, which is used to measure the severity of symptoms using a 4-point response scale: 0 = absolutely not, 1 = slight, 2 = moderately, and 3 = severely.

## Erectile Dysfunction

Patients completed the International Index of Erectile Function (IIFE-15) by themselves.[16] This is a short, self-applicable questionnaire that assesses erectile function (questions 1−5 and 15), orgasmic function (questions 9 and 10), intercourse satisfaction (questions 6 and 8), sexual desire (questions 11 and 12), and overall satisfaction (questions 13 and 14). IIFE was validated in the Brazilian context.[16] Screening positive for ED was defined by a score of 24 or less. IIEF-15 was adapted for use with MSM,[17] and in this version, screening positive for ED was defined by a score of 28 or less.[17] IIEF for MSM was translated to Portuguese by our research group, using translation validated instruments (Cronbach's alpha = 0,87).

## Premature Ejaculation

Premature ejaculation (PE) was assessed using IPE (Index of Premature Ejaculation)[18] translated and adapted to the Brazilian context.[19] The IPE is a self-report scale composed of 10 items that assess criteria such as the sense of control (4 items), sexual satisfaction (4 items), and distress (2 items). There is no established cutoff point for this index. For the current study, based on the DSM 5 criteria for PE, we adopted a cutoff value defined by questions 1 (sense of control), question 5 (sexual satisfaction), and questions 9 and 10 (distress). For each of these questions, the possible answers were: question 1 (1-almost always or always; 2-more than half the time; 3-half the time; 4-less than half the time; 5-almost never or never); question 5 (1-very satisfied; 2-satisfied; 3-neither satisfied nor dissatisfied; 4-dissatisfied; 5-very dissatisfied); questions 9 and 10 (1-deeply frustrated; 2-very frustrated; 3-moderately frustrated; 4-only slightly frustrated; 5-not at all frustrated). Patients scored 1 point if they answered 1 or 2 for each of these questions and scored zero if they answered 3, 4, or 5. If the final sum was more than 3, we considered that the patient screened positive for PE.

## Female Sexual Function

Female sexual function was assessed using Female Sexual Function Index (FSFI)[20] adapted to the Brazilian context.[21] The FSFI analyzes sexual function by assessing arousal, sexual desire, orgasmic function, overall satisfaction, and level of dyspareunia. Scores of 26 or less suggest screening positive for SD.

## Hypoactive Desire

We used the SD domain of FSFI to evaluate hypoactive sexual desire disorder. A previous study supports the diagnostic accuracy of the SD domain for use in observational studies and clinical trials of hypoactive sexual desire disorder.[22] Screening positive for hypoactive desire was defined by a total sum of 5 or less at domain I (question 1 + question 2) of the FSFI.

## Statistical Analysis

In descriptive statistics, categorical variables are presented as percentages. Parametric variables were expressed as means and standard deviation, and nonparametric variables as medians and interquartile ranges (25th and 75th percentiles). Association between demographic and clinical characteristics and each of the sexual function domains (ED, PE, FSD, and hypoactive female desire) were analyzed through univariate analysis in subsamples, namely, heterosexual men screening positive for ED, PE; MSM screening positive for ED, PE; women screening positive for FSD; hypoactive desire. Comparison among groups was carried out using the chi-squared test for categorical variables, the Mann−Whitney U test for 2 categories, and the Kruskal−Wallis test for 3 categories of numeric variables when variables had non-normal distribution.

The variables that were associated with any SD in the univariate analysis of subsamples or presenting clinical relevance were tested in the multivariate logistic regression, considering as the dependent variable, screening positive for any SD that we investigated through the IIFE-15, IPE or FSFI. The odds ratio (OR) of

screening positive for any SD was calculated with a 95% confidence interval (CI). A multivariate, logistic regression analysis was then performed including the whole sample. For the "any comorbidity" variable, we considered those who had diabetes, hypertension, or dyslipidemia; for the "any hormonal abnormality" variable, those who had any alteration in hormonal dosage and for the "current depression/anxiety" variable, those who were at risk in suffering depression or anxiety according to BDI-II and BAI. All these variables considered relevant were included as explanatory variables. STATA version 15 (College Station, TX, USA: StataCorp LLC) was used for the analysis. Throughout the analysis, a P value of less than 0.05 was considered statistically significant.

## RESULTS

Figure 1 present the frequencies of screening positive for SD on self-report measures. Sociodemographic and clinical characteristics are presented in Table 1. MSM was more likely to self-report as Caucasian when compared to women ($X^2$ = 7.35; $P$ = .007). MSM also reported more years of education (Md = 14; IQR 5−22) than women (Md = 11; IQR 0−23) and heterosexual men (Md = 11, IQR 1−22) (z = 4.78; $P$ < .001). More heterosexual men and women were engaged in a stable union as compared to MSM ($X^2$ = 36.90; $P$ < .001). More heterosexual men were in use of HIV protease inhibitors ($X^2$ = 5.98; $P$ =.014) and had detectable viral load ($X^2$ = 6.10; $P$ = .013) than MSM. Heterosexual men were more likely to have diabetes when compared to women ($X^2$ = 5.41; $P$ = .03). Heterosexual men got lower scores in BDI (Md = 4; IQR 0−38) in comparison to MSM (Md = 7; IQR 0−43) (z = -2.019; $P$ = .004) and women (Md = 9; IQR 0−50) (z = -2.99; $P$ = .002). Also, heterosexual men got lower score in BAI (Md = 4; IQR 0−38) than women (Md = 7; IQR 0−37) (z = -2.42; $P$ = .015). We found that women were less likely to present abnormal hormone levels in comparison to MSM and heterosexual men when we analyzed abnormal testosterone levels ($x^2$ = 6.27; $P$ = .023), abnormal oestradiol levels ($x^2$ = 14.55; $P$ < .001), abnormal prolactin levels ($x^2$ = 11.50; $P$ = .008) and abnormal follicle stimulating hormone (FSH) levels ($x^2$ = 6.61; $P$ = .03).

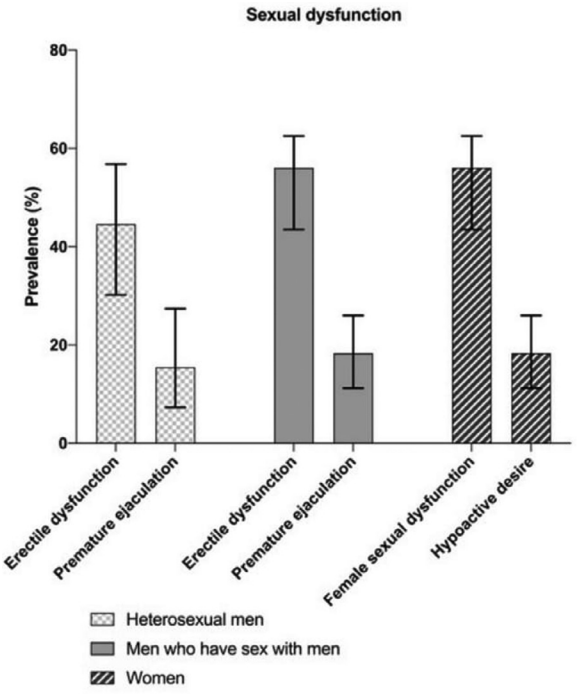


**Figure 1.** Prevalence of sexual dysfunctions according to gender and sexual orientation group.

In Table 2, we present factors associated with ED in the univariate analysis. Older age was associated with an increased risk for ED in MSM: among those who screened positive for ED, the median age was 50.5 years (IQR 45.1−55.5), whereas, among those who did not screen positive for ED, the median age was 45.1 years (IQR 36.9−54.2). Older age was also associated with higher risks of presenting FSD, with a median age of 53 years (IQR 49.5−55.2) among those who screened positive for FSD, as compared to the median age of 47.1 years (IQR 41−52) among those who did not screen for FSD. Among heterosexual men, we found higher ED and PE rates among those currently unemployed: 76% of those who were unemployed screened positive for ED, vs 26% among those who work; 33.3% from the unemployed group who screened positive for PE, and only 5.5% from those who worked who screened positive for PE. Unemployed women also showed a higher risk of screening positive for hypoactive desire; among those who did not work, 60% screened positive for hypoactive desire while 39% among those who worked screened positive for this issue. Time on ART was associated with screening positive for ED among heterosexual men, with a median time of therapy of 82.2 (IQR 38.4 −226.79) months among those who screened positive for ED and a median time of 216 (IQR 171.6−241.2) months among those who did not screen positive for ED. Being single was associated with an increased risk of FSD: among women in a stable union, 40% screened positive for FSD compared to 60% among those who were single.

Heterosexual men who screened positive for PE had a higher score in BAI (Md = 15, IQR 4−23) in comparison with those who did not screen positive for PE (Md = 3; IQR 1−10).

Depression was associated with an increased rate of screening positive for SD on self-report measures among all 3 groups. Among heterosexual men, those who screened positive for ED had a median BDI score of 7 (IQR 2−16), whereas those who did not screen it had a median score of 2 (IQR 0−9) ($P$ = .042); heterosexual men who screened positive for PE had a median of 16 (IQR 10−32) at BDI against a median of 3 (IQR 1−9) among those who did not screen it ($P$ = .006). MSM who screened positive for PE got a higher score at BDI (Md = 8, IQR 4−16.5), as compared to those who did not screen for PE

**Table 1.** Demographic and clinical characteristics of study participants, according to gender/sexual orientation group

| | Heterosexual men (*N* = 58) Md (IQR) | Men who have sex with men (*N* = 113) Md (IQR) | Women (*N* = 63) Md (IQR) | *P*-value |
|---|---|---|---|---|
| Demographics | | | | |
| Age, y | 51.4 (45.5–54) | 49.4 (41.6–55) | 48.5 (42–53.5) | .431 |
| White/Caucasian race (%) | 34 (59) | 74 (65) | 28 (44) | .025* |
| Years of education | 11 (7–11) | 14 (11–16) | 11 (8–12) | <.001† |
| Income, Brazilian reais | 2500 (780–5000) | 3000 (900–6000) | 2500 (1300–4000) | .460 |
| Currently unemployed | 21 (36) | 36 (32) | 28 (44) | .184 |
| Currently in stable union | 33 (57) | 16 (14) | 28 (44) | <.001† |
| HIV-related variables | | | | |
| Months since HIV diagnosis | 209 (82–257) | 208 (149–242) | 222 (175–248) | .615 |
| Under antiretroviral therapy | 56 (97) | 109 (96) | 63 (100) | .372 |
| Months on HAART use (Md, IQR) | 192 (79.1–235.2) | 192 (106.8–229.2) | 201.6 (130.8–229.2) | .738 |
| Antiretroviral regimen base | | | | |
| NNRTI | 16 (28) | 51 (45) | 22 (35) | .065 |
| Integrase inhibitor | 6 (10) | 6 (5) | 10 (16) | .063 |
| Protease inhibitor | 34 (59) | 44 (39) | 31 (49) | .046‡ |
| Detectable HIV viral load | 10 (17) | 7 (6) | 5 (8) | .049‡ |
| CD4 count | 584 (419–750) | 659 (467–921) | 702 (332–889) | .264 |
| Any comorbidity | 39 (67) | 87 (77) | 43 (68) | .288 |
| Hypertension | 16 (27) | 33 (29) | 15 (24) | .743 |
| Dyslipidemia | 26 (45) | 52 (46) | 26 (41) | .829 |
| Diabetes | 12 (20) | 19 (17) | 4 (6) | .050‖ |
| Mental health | | | | |
| Beck depression score | 4 (1–11) | 7 (3–15) | 9 (4–16) | .011§ |
| Beck anxiety score | 4 (1–13) | 6 (2–11) | 7 (4–13) | .045‖ |
| Hormone levels | | | | |
| Testosterone (ng/dL) | 541 (422–714) | 489 (382–636) | 12 (12-20) | |
| Abnormal levels (%) | 9 (16) | 13 (12) | 0 (0) | .023¶ |
| Progesterone (ng/mL) | - | - | 0.3 (0.3–0.5) | |
| Abnormal levels (%) | | | 0 (0) | |
| Oestradiol (pg/mL) | 29.5 (22.0–36.8) | 27.6 (20.4–37.5) | 28.7 (15.0–101.0) | |
| Abnormal levels (%) | 19 (33) | 40 (35) | 2 (3) | <.001¶ |
| Prolactin (ng/mL) | 8.1 (6.0–11.9) | 7.4 (5.3–10.7) | 10.0 (6.0–13.7) | |
| Abnormal levels (%) | 3 (5) | 7 (6) | 9 (14) | .008¶ |
| S-HBG (nmol/L) | 62.7 (47.5–77.8) | 50.8 (35.7–68.7) | 89.0 (56.1–129.8) | |
| Abnormal levels (%) | 16 (28) | 33 (29) | 10 (16) | .909 |
| FSH (IU/L) | 7.8 (4.6–12.2) | 6.6 (3.5–9.6) | 41.8 (10.9–68.3) | |
| Abnormal levels (%) | 12 (21) | 14 (12) | 1 (2) | .030¶ |
| Any abnormal hormone measurement (%) | 36 (62) | 69 (61) | 18 (29) | .151 |

Numeric variables are presented as medians and interquartile range. Hormonal levels missing for up to 56 patients.
*statistically significant difference in pairwise comparison between men who have sex with men and women.
†statistically significant differences in pairwise comparison between men who have sex with men and women and between men who have sex with men and heterosexual men.
‡statistically significant difference in pairwise comparison between men who have sex with men and heterosexual men.
§statistically significant differences in pairwise comparison between men who have sex with men and heterosexual men and between heterosexual men and women.
‖statistically significant difference in pairwise comparison between heterosexual men and women.
¶*P* > .05 in pairwise comparison between men who have sex with men and heterosexual men.

**Table 2.** *P*-values for univariable analysis of variables associated screening positive for sexual dysfunction among people living with HIV, according to gender/sexual orientation group

| | Heterosexual men *N* = 58 | | Men who have sex with men *N* = 113 | | Women *N* = 63 | |
|---|---|---|---|---|---|---|
| | Erectile dysfunction | Premature ejaculation | Erectile dysfunction | Premature ejaculation | Female sexual dysfunction | Hypoactive desire |
| Age | 0.94 | 0.92 | **0.03** | 0.15 | **0.007** | 0.06 |
| White/Caucasian race | 0.23 | 0.46 | 0.34 | 0.30 | 0.35 | 0.67 |
| Years of education | 0.24 | 0.31 | 0.07 | 0.50 | 0.91 | 0.61 |
| Income | 0.15 | 0.80 | 0.17 | 0.26 | 0.98 | 0.94 |
| Current unemployment | **<0.001** | **0.009** | 0.41 | 0.17 | 0.55 | **0.04** |
| Stable union | 0.93 | 0.71 | 0.98 | 0.73 | **0.01** | 0.53 |
| Months since HIV diagnosis | 0.10 | 0.93 | 0.44 | 0.30 | 0.23 | 0.19 |
| Antiretroviral use | 1.00 | 1.00 | 0.58 | 0.56 | - | - |
| Months on HAART use | | | | | | |
| Antiretroviral regimen base | **0.02** | 0.76 | 0.16 | 0.47 | 0.64 | 0.67 |
| NNRTI | 0.26 | 0.05 | 0.67 | 0.55 | 0.98 | 0.57 |
| Integrase inhibitor | 0.39 | 0.23 | 0.06 | 0.22 | 0.08 | 0.16 |
| Protease inhibitor | 0.07 | 0.72 | 0.21 | 0.33 | 0.77 | 0.61 |
| Detectable HIV viral load | 0.26 | 1.00 | 0.21 | 0.10 | 0.64 | 0.16 |
| Any comorbidity | 0.59 | 0.69 | 0.31 | 0.08 | 0.77 | 0.70 |
| Hypertension | 0.08 | 0.09 | 0.12 | 1.00 | 0.42 | 0.84 |
| Dyslipidemia | 0.83 | 1.00 | 0.29 | 0.61 | 0.93 | 0.50 |
| Diabetes | 0.67 | 1.00 | 0.43 | 0.25 | 1.00 | 1.00 |
| Beck anxiety score | 0.08 | **0.02** | 0.99 | 0.15 | 0.54 | 0.28 |
| Beck depression score | **0.04** | **0.006** | 0.06 | **<0.001** | 0.47 | **0.01** |
| Testosterone (ng/dL) | **0.009** | 0.12 | 0.56 | 0.65 | 0.14 | 0.07 |
| Abnormal testosterone | 0.71 | 0.62 | 0.92 | 1.00 | - | - |
| Oestradiol (pg/mL) | 0.11 | 0.14 | 0.82 | 0.22 | **0.009** | **0.04** |
| Abnormal oestradiol | 0.20 | 0.27 | 0.87 | 0.35 | 0.52 | 0.67 |
| Prolactin (ng/mL) | **0.01** | **0.04** | 0.13 | 0.87 | 0.07 | 0.14 |
| Abnormal prolactin | 0.25 | 1.00 | 0.67 | 0.11 | 0.25 | 1.00 |
| SHBG (nmol/L) | 0.16 | 0.31 | 0.46 | 0.48 | 0.69 | 0.36 |
| Abnormal SHBG | 0.28 | 0.69 | 0.36 | 0.50 | 0.68 | 0.56 |
| FSH (IU/L) | 0.95 | 0.10 | 0.19 | 0.13 | **0.01** | **0.04** |
| Abnormal FSH | 0.41 | 0.42 | 0.23 | 0.25 | 0.31 | 1.00 |
| Any abnormal hormonal measurement | 0.50 | 0.65 | 0.57 | 0.08 | 1.00 | 1.00 |

Data in boldface means those results which the p value is equal or minor than 0.05.

(Md = 5; QR 2−12). Among women, those who screened positive for hypoactive desire got a median of 11.5 (IQR 7.5−22.5) at BDI, and those who did not screen positive for hypoactive got a median of 6.5 (IQR 4−11) (*P* = .012). Lower testosterone levels were associated with an increased risk of screening positive for ED among heterosexual men; those who screened positive for ED had a median of 483.5 (IQR 343−564) in comparison to a median of 641 (IQR 486−732) among those who did not screen for ED. Women screening positive for SD presented lower levels of oestradiol (Md = 15, IQR 15−15) compared to those who did not screen positive for SD (Md = 37.5; IQR 15−125.2) (*P* = .009). FSH levels were higher among women who screened positive for SD. Heterosexual men with ED got lower levels of prolactin (Md = 6.25; IQR 5.15−8.35) as compared to those who did not screen positive for ED (Md = 8.4; IQR 7.9−13) (*P* = .015). Furthermore, heterosexual men who screened positive for PE presented lower levels of prolactin (Md = 6.5; IQR 5.3−8) compared to those who did not screen positive for PE (Md = 8.3; IQR 6.2−12.1). Women who screened positive for SD showed higher levels of FSH (Md = 0.018; IQR 55−70.3) in comparison with those who did not screen positive for SD (Md = 24.9; IQR 5.6−59.7). Women screening positive for hypoactive desire presented higher levels of FSH (Md = 57.8; IQR 38−66.4) compared to those who did not screen positive for hypoactive desire (Md = 22.95; IQR 4.5−70.3).

In Table 3, we present the logistic regression models of SD, including the whole sample. Age, MSM, presenting current depression/anxiety, and the use of protease inhibitors were shown to be independent predictors of SD adjusting for presenting any comorbidity and any hormonal abnormality.

**Table 3.** Multivariable analysis of factors associated with screening positive for sexual dysfunction among people living with HIV (n = 177)

| | Model 1 OR (95% CI) | *P*-value | Model 2 OR (95% CI) | *P*-value |
|---|---|---|---|---|
| Age | 1.039 (1.002–1.078) | .038 | 1.041 (1.004–1.078) | .026 |
| Sex/orientation group | | | | |
| Heterosexual men | Referent | - | - | - |
| MSM | 2.278 (1.034–5.017) | .041 | 2.655 (1.228–5.739) | .013 |
| Women | 1.390 (0.508–3.802) | .520 | 1.538 (0.576–4.106) | .389 |
| Any comorbidities | 1.306 (0.578–2.950) | .521 | 1.322 (0.596–2.932) | .491 |
| Any hormonal abnormality | 1.621 (0.786–3.344) | .191 | 1.603 (0.786–3.270) | .194 |
| Current depression/anxiety | 2.968 (1.498–5.877) | .002 | 2.957 (1.516–5.768) | .001 |
| Use of protease inhibitor | 0.419 (0.241–0.819) | .011 | - | - |

## DISCUSSION

To the best of our knowledge, this is the first study on the frequency of screening positive for SD on self-report measures and associated factors in a cohort of PLHIV who have been in treatment using ART for a significant amount of time.

The chance of screening positive for ED in our study was 49.7% (44.6% among heterosexual men and 56% among MSM) and the median time on ART was 192 months among men (IQR 80.4–230.39). In similar studies, the prevalence of ED was found to be 53.2% in a population with a median use of ART of 119 months (IQR 61–188)[23] and 54.5% in a population with a median use of ART of 109 months (IQR 79–142).[24] Likewise, a prevalence of ED of 53.4% was found in a study where participants had less time of exposure to ART (M = 66.4 months; SD = 42.4)[13] and a 64% prevalence of ED was found among HIV patients with average exposure to ART of 55.9 (SD = 44.1) months.[25] Once long-term exposure to ART is found to be strongly associated with ED,[11] we would expect a higher frequency in our sample, as compared to findings of other studies involving patients with shorter exposure to ART, but, surprisingly, the frequency found was very similar or even lower. This may be related to good adherence to treatment found in our sample, given that patients regularly visit clinicians, resulting in greater control of HIV disease progression and more frequent assessment of comorbidities, including SD.

The chance of screening positive for PE was 16.9% (15.5% in heterosexual men and 18.3% in MSM). The few studies on PE in PLHIV rarely used standardized instruments.[2] In one study, 18% had IPE scores that suggest PE, [26] but time on ART was not specified. PE seems to be more present in HIV-positive MSM when compared to their seronegative counterparts.[27]

In previous studies, a prevalence of 32% of SD was found in a sample with a median use of NRTI (HIV nucleoside reverse transcriptase inhibitors) of 112 months.[28] Another study reported a 34.4% of FSD and a median time of 108 months (IQR 48–144) on ART.[29] Such prevalence of FSD is similar to those found in previous studies, even though in none of these studies women had been under ART for such a long time. In our study, the prevalence of FSD was 27.4%, and 45.1% of them presented hypoactive desire. Being single was associated with an increased risk of FSD: among women in a stable union, 40% presented FSD compared to 60% among those who were single. The median time on ART among females was 201.6 months (IQR 130.8–229.2). FSD was found to be highly frequent among our cohort of women infected with HIV. These data point out that perhaps a significant part of these women are presenting a poor quality of sexual life, which may reflect on their mental health. Healthcare providers must be aware of the importance of initiating conversations around sexuality during post-test counseling and regular appointments, as well as offering support for challenges that may be distressing to women. We understand that the discussion around SDs in women with HIV must be thought beyond the perspective of a health problem, emphasizing the importance of women's pleasure to achieving sexual health and rights, aligned with international reports.[30]

In this study, we analyzed a middle-aged population, composed mainly of Caucasians, with a high educational level and high income compared to the Brazilian population average. Most of them had good adherence to treatment, with stable HIV control parameters. Such characteristics may be related to the location of the outpatient clinic and the type of follow-up that prioritizes a comprehensive approach to the patients' health. Age and unemployment were related to sexual difficulties. Older age is a well-known risk factor for SD both in the general population and in PLHIV.[4,8,31] Unemployment as an associated factor can be explained by how financial difficulties in general impact quality of life, exposing the individual to situations of greater social vulnerability and impacting sexual health.

In our study, anxiety and depression were relevant, with depression being highly associated with SD for all 3 groups. Associations between anxiety and depression and SD were also found in previous studies.[8,9,11] Depression and psychological distress have been established as factors relevant to SD regardless of HIV status,[32] and studies show that there is a higher prevalence of depression among PLHIV.[33] The overlap between symptoms related to HIV infection and symptoms related to depression and

anxiety may be a challenge to correctly diagnose psychiatric symptoms in clinical practice. In PLHIV, psychological distress and risky sexual behaviors may enhance anxiety.[26] In our cohort, the prevalence of risk of depression was 35 % (33.5% for men and 39.6% for women). For a general sample of PLHIV, the polled prevalence estimates were 50.8% for depression or depressive symptoms.[34] In another study, a prevalence of 32% of depression was found, and the average time on ART was 56.8 months.[35]

For heterosexual men, lower total testosterone levels and lower prolactin levels were found to be associated with SD. ED and hypogonadism are commonly clinical conditions found in HIV-infected men. Hypogonadism can be manifested as osteoporosis, SD, decreased libido, reduced body mass, and depression.[36] Likewise, such symptoms of hypogonadism can overlap with those of HIV infection.[37] In middle-aged and elderly men without HIV low prolactin levels are related to psychological symptoms, unhealthy metabolic phenotypes, and SD[38]; these findings may indicate how low prolactin levels impact sexual health in PLHIV. For women, our study suggested that lower levels of oestradiol and higher FSH levels were related to SD and lower levels of sexual desire.

In the multivariable analysis comprising the whole sample, age, anxiety, and depression were associated with screening positive for any SD. MSM were at higher risk for SD, and the use of HIV protease inhibitors was found to be a protective factor.

MSM and PLHIV present higher rates of SD.[26] Health disparities are still a factor relevant to MSM, leading to poor health conditions.[39–41] This could be better understood using the syndemic theory framework, defined by the interaction of multiple conditions and psychosocial risk factors that work synergistically increasing the risk of negative health outcomes.[42] The syndemic theory describes a situation in which adverse conditions common among MSM, such as depression, fear of passing on HIV, risky sexual behaviors, and direct effects of HIV on the physiologic systems responsible for penile erection,[7,41,43] co-occur and amplify the risk of SD.

Previous studies found that depression was associated with SD among PLHIV,[9,11,44] though the specific mechanism is still not entirely clear.

One possible explanation is the potential negative effect of depression on HIV progression,[44] associated with SD. The connection between depression and HIV progression may involve biological, behavioral, and environmental variables. Depression can lead to chronic cortisol release,[45] decrease immune functioning, lower medication adherence, and consequently jeopardize optimal treatment effects. Moreover, depressive symptomatology is associated with high-risk sexual behavior,[44,46] increasing the risk of contracting other sexually transmitted viruses, which may worsen the clinical condition of PLHIV and their sexual health.

The role of HIV protease inhibitors on SD is still controversial. Surprisingly, we found a protector effect of using such medication to the occurrence of SD, whereas previous studies showed the opposite association or no association.[4,13] Future studies will likely be able to replicate this investigation considering samples under prolonged use of ART. A protector effect may be present just after a long time of using them.

This study has many strengths. This is the first study to analyze PLHIV in long-term treatment with ART. Secondly, we used standardized instruments to measure SD and collected blood samples to analyze hormonal variables for the best accuracy of the data. Thirdly, we analyzed SD and associated factors for each group separately (heterosexual men, MSM, and women) as there are particularities of sexual behavior for each group. Otherwise, there are some limitations to point out. Unfortunately, we interviewed patients that were followed up at a single outpatient clinic, which means that the sample is not representative of PLHIV in the entire city. Also, not all participants followed the instructions to go to the lab and collect blood exams, because of this, it was not possible to analyze the sexual hormone levels of the entire sample. The role of HIV stigma on SD was not included in this study although we consider its importance. Another limitation is related to the use of IIEF-15 for MSM, this measure was not validated in the Brazilian context, but our research group used validated translation tools and calculated Cronbach's alpha values. For building the main outcome "screening positive for any SD" we drew data from different measures with different psychometric properties. Despite we used some of the most used and psychometrically tested measures in the field, more studies should be done to test our findings. Finally, our study did not explore the segment of women with homo and bisexual orientation. Future studies should address the variables associated with SD in women according to sexual orientation.

## CONCLUSION

Despite receiving comprehensive health care at a reference outpatient clinic and presenting good adherence to treatment, PLHIV in our cohort presented alarming rates of depression and anxiety, which in turn is correlated with sexual and physical health problems. An important implication for clinicians is to specifically evaluate symptoms of depression and anxiety, as there is an overlap between these symptoms and HIV infection manifestations (Figure 1, Table 3).

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