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Prevalence and factors associated with sexual dysfunction among HIV-positive women in Europe

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Abstract *Little is known on female sexual dysfunction (FSD) among HIV-positive women. A cross-sectional survey in seven European HIV centres was performed and data on medical history, antiretroviral treatment and laboratory results were collected. Sexual function was evaluated by the Female Sexual Function Index (FSFI). The data from 166 women were available (response rate = 77%). The non-respondents had a lower CD4 cell count, were older and more frequently of sub-Saharan African origin. The overall median FSFI was 25.2 (interquartile range = 19.3). Thirty-six women (25%) had a FSFI score ≤ 10. Depression, irritability and anxiety were associated with a low FSFI score. The participants reported a significant decrease in sex functioning since HIV diagnosis but not since the start of antiretroviral treatment. Sexual dysfunction in women with HIV infection is frequent and is mainly driven by psychological factors and by the HIV diagnosis.*

Introduction

Female sexual dysfunction (FSD) is frequent in the general population (Dunn *et al.*, 1998; Laumann *et al.*, 1999) or in women attending STD clinics (Goldmeier *et al.*, 1997) and is clearly associated with a decrease in quality of life (Laumann *et al.*, 1999). FSD is a complex phenomenon that can be subdivided into desire, arousal, orgasmic and sexual pain disorders. Causes of FSD include vascular, neurologic, endocrine and/or psychological disorders (Phillips, 2000). Some objective methods exist to assess the sexual response but they are generally not standardized and not usable in daily clinical practice (Berman *et al.*, 1999b). Recently, validated scores using self-report techniques have been developed for the

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assessment of FSD (Rosen *et al.*, 2000). These scores can be used as endpoints in clinical trials as well as for diagnostic purposes.

There are many reasons to expect an increase in sexual dysfunction in HIV-positive individuals. Among others, psychological, endocrine (Dobs *et al.*, 1988; Rabkin *et al.*, 1995) and neurologic (Ali *et al.*, 1994; Di Rocco, 1999) factors seem the most important ones. There have been several studies evaluating sexual dysfunction in HIV-positive men (Collazos *et al.*, 2002; Colson *et al.*, 2002; Schrooten *et al.*, 2001) but very few on sexual functioning of women living with HIV/AIDS. Some early studies conducted before the broad use of highly active antiretroviral treatment (HAART) indicated high rates of sexual dysfunction among HIV-positive women (Goggin *et al.*, 1998; Meyer-Bahlburg *et al.*, 1993).

In two studies low sexual desire was seen in 41% (Brown *et al.*, 1993) and 39% (Goggin *et al.*, 1998) of HIV-positive women examined. In the latter report low sexual desire was related to the presence of depressive symptoms but not to low androgen levels.

The main objective of this study was to determine the frequency of sexual dysfunction among HIV-positive women attending HIV clinics in Europe. The secondary goal was to identify risk factors for the development of FSD.

Methods

HIV-positive women attending treatment centres at seven sites throughout Europe were invited to participate in the study between September 2000 and May 2002. Two questionnaires were administered. The first was completed by the physician or research worker and examined aspects of the medical history, current and previous antiretroviral treatment and laboratory results (total cholesterol, LDL-cholesterol, triglycerides and blood sugar levels). The second questionnaire, available in six languages, was given to the participant to complete at home. This contained questions to assess sexual function and other symptoms. Individuals were asked to return this questionnaire by post to the coordinating centre. A code was used to link this questionnaire to the data collected by the physician. To participate in the study, patients had to be older than 18 years, diagnosed seropositive for more than six months and to be able to read, understand and fill in the questionnaire independently.

The Female Sexual Function Index (FSFI; Rosen *et al.*, 2000) was used to evaluate sexual functioning. This standardized questionnaire evaluates six domains of female sexual functioning during the last four weeks: desire, arousal, lubrication, orgasm, satisfaction and pain during sexual intercourse. A higher score indicates a better sexual functioning; the maximum score cumulating the score of each domain is 36. This score is described as a continuous variable; no categories based on severity of FSD are described.

Current HIV treatment was defined as the antiretroviral therapy being taken at the time the questionnaire was completed. For the purpose of analysis combinations were categorized as one of the following: protease inhibitor (PI) and nucleoside analogues (NRTI), non-nucleoside analogues (NNRTI) and NRTI, a combination of the three classes (PI+NNRTI +NRTI) and NRTI only. Previous treatment was any antiretroviral treatment taken since HIV diagnosis but not included in the current regimen. Lipodystrophy was defined as having at least one of the following symptoms confirmed by clinical examination: increase in abdominal girth or breast volume, or fat accumulation in the neck (hypertrophy symptoms); decrease of fat in the face, over the buttocks area or on the limbs (atrophy symptoms). Signs of psychological distress (depression, irritability and anxiety) were defined by patients' self-assessment.

Comparison of sexual function scorings between different groups was done using non-parametric tests (Mann-Whitney U test, Kruskal-Wallis test). Non-parametric correlation test (Spearman Rank) was used to detect correlation between ordinal variables and sexual function scorings. *P*-values lower than 0.05 were considered statistically significant.

All analyses were performed using the SPSS software packet version 10.0.

Respondents were not compensated financially or by other means. All women gave informed consent and local ethics committees approved the study protocol.

Results

Population characteristics

Two hundred and fifteen questionnaires were distributed and 166 were completed (response rate = 77%). Most of the women were Caucasian and were infected through heterosexual contact; on average they were 36 years old and had been diagnosed HIV-positive for 7.2 years (see Table 1). Most of the women were currently using antiretroviral treatment ($n = 131$, 79%); less than a quarter were antiretroviral naive ($n = 35$, 21%). At the time of the survey, most of the women were taking PI-containing regimens ($n = 54$; 41% of the women taking therapy) or NNRTI-containing regimens ($n = 42$; 32%). Only a minority of women were taking a PI- and NNRTI-containing treatment ($n = 5$; 4%) or a combination of NRTI only ($n = 12$; 11%). The median duration of the current therapy regimen was 11.5 months, while the mean duration of total exposure to antiretroviral therapy was 38 months.

There were more Black African woman among the non-respondents than among the respondents (15 (40%) versus 16 (10%); $p < 0.001$). Non-respondents were significantly older than respondents (median age = 38.5 years versus 36 years, $p = 0.027$ and had a

Table 1. *Characteristics of study participants*

Characteristic	
Age (years)	36.0 (8.0)
BMI (kg/m^2)	22.2 (4.9)
Exposure risk	
Heterosexual contacts	103 (62.0%)
Injecting drug use	34 (20.5%)
Other	29 (17.5%)
Origin	
Caucasian	138 (83%)
Others	28 (17%)
Time since first positive HIV test (years)	7.2 (7.3)
CDC stage	
A	85 (51.2%)
B	43 (25.9%)
C	38 (22.9%)
Current CD4 level	
<50 cells/mm^3	1 (0.6%)
50–200 cells/mm^3	14 (8.5%)
200–500 cells/mm^3	55 (33.3%)
>500 cells/mm^3	95 (57.6%)

If not specified values are expressed as median (interquartile range).
BMI = body mass index.

significantly lower CD4 lymphocyte count (450 cells/mm^3 versus 572 cells/mm^3, $p=0.021$). There were no differences in HIV transmission mode, exposure to antiretroviral treatment, co-morbidity and time since HIV diagnosis between respondents and non-respondents (data not shown).

The prevalence of concomitant pathologies that could potentially lead to sexual dysfunction was low. One woman (0.6%) had diabetes mellitus, six (3.6%) arterial hypertension, 16 (9.6%) neuropathy and two (1.2%) a psychiatric disease. More than three-quarters of the women were currently smoking ($n=127$, 77%), for a mean duration of 15 years and on average 16 cigarettes per day. Seventy-one women (43%) reported alcohol use, on average five units per week. Twenty-two women (13%) reported substance abuse or substitution therapy, which included cannabis ($n=11$), cocaine ($n=5$) and methadone ($n=3$). At the time of the survey a small number of women were using co-medication known potentially to interfere with sexual functioning such as antidepressants (2%) and antihypertensive drugs (4%).

Sexual functioning during the last 4 weeks

The overall median total score on sexual functioning (sum of the different domains) over the last four weeks was 25.2 (interquartile range 19.3) (see Table 2). The overall satisfaction in the sexual relationship was the most affected domain of sexual functioning in both ARV experienced and naive women; scores on physical symptoms of sexual dysfunction such as lubrication problems and pain were high. The study population seemed to be composed of two sub-populations (see Figure 1): the first one with a score under ten ($n=36$; 25% of the population) with a higher grade of SD; the second one with a score above 24 with no or mild SD ($n=81$; 56.3% of the population). A significant lower sexual functioning score was observed among women who reported to suffer from depression ($p=0.015$), irritability ($p=0.011$) or anxiety ($p=0.07$). Using univariate analysis, no significant associations were found between sexual functioning scores and age, ethnic origin, HIV transmission mode, time since HIV diagnosis, cigarette, alcohol and drug use, current CD4 lymphocyte count and viral load level, or previous and current exposure to antiretroviral drugs. Sexual dysfunction was not associated with any ARV in particular or HIV treatment combination. Laboratory results were available for a sample of women: total cholesterol ($n=162$), LDL-cholesterol ($n=112$), triglycerides ($n=160$) and blood sugar levels ($n=160$). No significant relations were found between sexual functioning scores and those parameters. Around one-third ($n=41$; 31.3%) of

Table 2. *Sexual functioning during the last four weeks: FSFI score of antiretroviral naive and antiretroviral-treated women*

Sexual functioning		All participants	ARV naive	ARV treated	
	n	166	35	131	
Domain	range	Median (IQR)	Median (IQR)	Median (IQR)	*p*
Desire	1.2 to 6	3.6 (2.4)	4.2 (2.4)	3.6 (1.8)	0.225
Arousal	0 to 6	4.4 (4.4)	4.5 (5.1)	4.2 (4.1)	0.327
Lubrication	0 to 6	5.1 (6.0)	4.4 (5.7)	5.1 (5.6)	0.178
Orgasmic function	0 to 6	4.8 (5.6)	2.4 (5.5)	4.8 (4.6)	0.082
Satisfaction	0.8 to 6	2.4 (2.0)	2.6 (2.1)	2.4 (2.0)	0.335
Pain	0 to 6	5.2 (6.0)	4.0 (6.0)	5.8 (3.7)	0.075
Total score	2 to 36	25.2 (19.3)	19.8 (21.3)	25.4 (14.4)	0.214

N=number of observations; IQR=interquartile range; ARV=antiretroviral treatment.

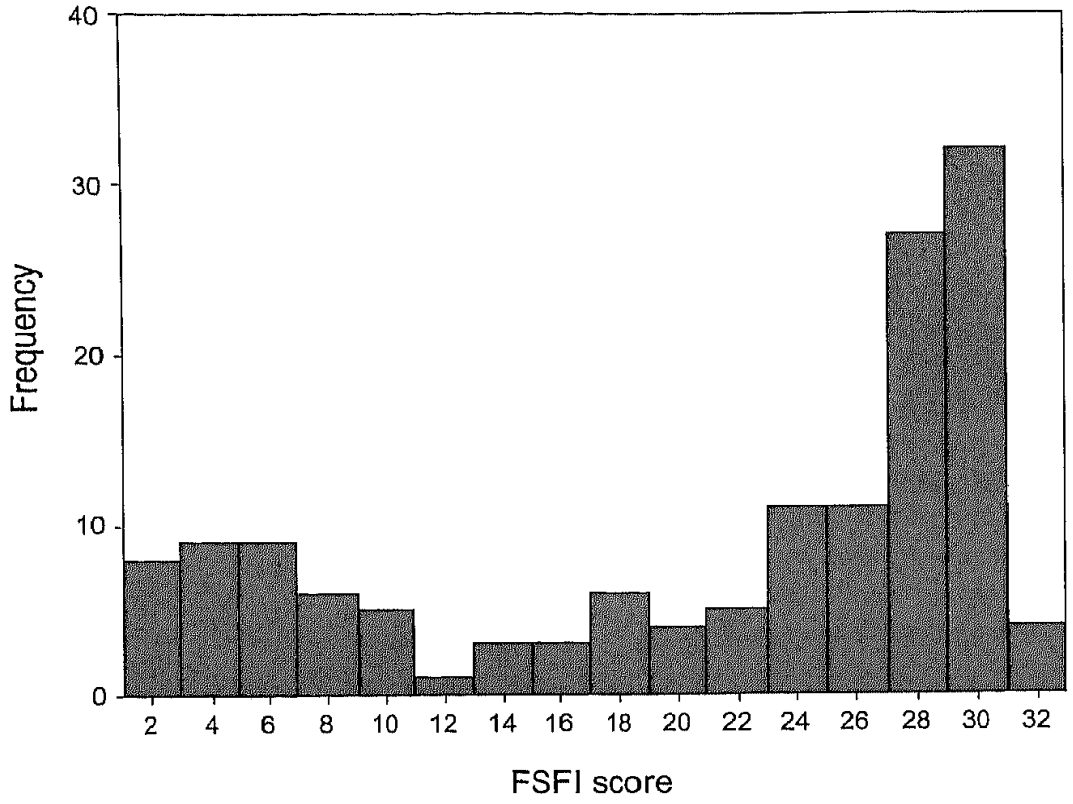

FIG. 1. *Distribution of the female sexual function index (FSFI).*

the women who were taking antiretroviral treatment presented signs of lipodystrophy (LD). Twenty-six (63.4%) had at least one lipo-atrophy sign and 33 (80.5%) at least one lipo-hypertrophy sign. No significant association between sexual functioning score and the presence of LD or a sub-type of LD (atrophy or hypertrophy) was found.

A multivariate analysis was not performed considering the lack of statistically significant variables in the univariate analyses.

In total, 49 women (29.5%) reported attempts to improve their sexual life. The different interventions included psychological help ($n=36$; reported success rate $=31\%$), changing antiretroviral treatment ($n=25$; reported success rate $=12\%$) and stopping antiretroviral treatment ($n=25$; reported success rate $=16\%$).

Evolution of sexual functioning

Three questions were used to investigate retrospectively the evolution of sexual functioning in three domains: the sexual desire, the level of arousal and the orgasmic function. A significant decrease was found in all three domains before and after HIV diagnosis (see Table 3). No significant difference was found when comparing the different domains before and after start of antiretroviral treatment.

Discussion

This is the first report of sexual functioning among HIV-positive women in the HAART era. A quarter of the participants reported moderate to severe sexual dysfunction. No particular sexual disorder was dominant. The FSD prevalence is highly variable in the general population, ranging from 9% (Goldmeier *et al.*, 1997) to 63% (Frank *et al.*, 1978), according

Table 3. *Evolution of sexual functioning: prior to HIV diagnosis, before and during antiretroviral (ARV) treatment*

Score (maximum = 5)	Degree of sexual desire	*p*	Level of arousal	*p*	Frequency of orgasm	*p*
Prior to HIV diagnosis	3.4		3.5		3.8	
Before ARV treatment	2.8	<0.001	2.8	<0.001	3.2	<0.001
During ARV treatment	2.7	0.28	3	0.18	3.4	0.15

p-value for comparison with one level above.

to the definition and methodology used. FSD is also common among women suffering from chronic diseases where it is unclear whether sexual problems are caused by the disease, its treatment or psychogenic factors. Using a validated self-administered questionnaire, FSD was described among 43% of 67 women suffering from arterial hypertension (Burchardt *et al.*, 2002) and in 27% of 120 women suffering from type I diabetes (Enzlin *et al.*, 2002).

In our study, psychological distress was the only risk factor associated with FSD. Depression was also the only risk factor for FSD described in a cohort of diabetic women (Enzlin *et al.*, 2002). The cross-sectional design of our study, however, did not allow a causal interpretation of this observation. The link between HIV infection and psychological distress seems straightforward and the association between mood disorders and FSD has already been described (Baldwin, 2001).

Our study results should be interpreted with caution: indeed, our study participants cannot be considered to be representative of all HIV-positive women in Europe. Moreover, recall of pre-HIV or early-on diagnosis feelings may not be accurate. Indeed, it is well documented that current mood affects recall (depressed people recall things more negatively, for example).

Sexual dysfunction has been previously associated with the use of antiretroviral drugs, especially the protease inhibitors (Collazos *et al.*, 2002; Colson *et al.*, 2002; Schrooten *et al.*, 2001), although this association is still controversial (Lallemand *et al.*, 2002). Others have described an increased satisfaction with sexual life during NNRTI treatment (Murri *et al.*, 2003) or after switching from a PI- to a NNRTI-containing regimen (Colebunders *et al.*, 2001). Those studies were mostly performed in men and did not always include a control group of naive patients. In this study no single antiretroviral or treatment combination was found to be associated with FSD. Attributing an influence of antiretroviral drugs on FSD may however be difficult when combinations of drugs are used and when most individuals have had sequential exposure to antiretroviral drugs.

No association between lipodystrophy (LD) and FSD was found, which is in contrast with results of a recent study from Italy (Trotta *et al.*, 2003). One may expect that LD could lead to FSD due to changes in body image. Others have suggested that conversion of testosterone in oestrogen in the atrophy area of lipodystrophic persons could lead to a low testosterone state facilitating FSD (Goldmeier *et al.*, 2002).

Previous studies have demonstrated that decreases in sexual functioning are associated with being diagnosed HIV-positive (Brown *et al.*, 1993). Responses in this study to questions asking women to recall whether changes occurred over time support these other studies, although we recognize this methodology is subject to bias. In order to eliminate this, prospective studies are required. While it would be difficult to capture a population before and after HIV diagnosis, evaluation during the untreated phase and then following the introduction of antiretroviral treatment would allow more effective assessment of any treatment effect, particularly if this were in the setting of randomized studies.

Additional factors such as partnership, marital and family planning status, parity, education level, HIV disclosure and HIV seroconcordancy/discordancy between partners may all be important to consider in future studies.

Compared to other studies, the response rate achieved was reasonable (Burchardt *et al.*, 2002). The different characteristics of those in the non-responding group do mean however that care needs to be taken in generalizing the results of this study across all groups of women attending treatment centres. Further work exploring why there might be differences in response, particularly amongst minority ethnic groups, is necessary.

In conclusion, FSD is frequent among HIV-positive women. Antiretroviral treatments do not seem to play an important role in this syndrome, which is probably mainly driven by psychological factors. Sexual function of HIV-positive women should be regularly investigated in daily clinical practice by standardized and validated tools. In order to realize this objective, a comprehensive approach (Berman *et al.*, 1999a) including all members of a multidisciplinary team may be useful.

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