Evaluation of sexual function and depression in married women with interstitial lung diseases
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\textbf{Background} Little is known about female sexual function and interstitial lung disease (ILD). The purpose of this study was to evaluate sexual function and depression in married women with ILD.

\textbf{Patients and methods} Of the 65 participants enrolled, 45 patients with ILD fulfilled the inclusion criteria, comprising 12 patients with idiopathic pulmonary fibrosis, 25 with connective tissue disease-associated interstitial pneumonias, eight patients with other interstitial pneumonias. Moreover, 20 age-matched normal individuals were recruited as controls. All participants were evaluated for clinical data, including age, BMI, comorbidities, duration of ILD, usage of glucocorticoids (dose and duration), and number of exacerbation within the past year. All women fulfilled the female sexual function index (FSFI) and Beck depression inventory.

\textbf{Results} The mean age of the ILD group was 40.4±8.9 years. Overall, 33.3\% were hypertensive and 53.3\% had pulmonary hypertension, whereas diabetes mellitus and dyslipidemia were found in 26.6 and 15.5\%, respectively. The mean duration since diagnosis of ILD and using glucocorticoids was 8.46±2.77 and 9.23±2.31 years. No differences in forced vital capacity and forced expiratory volume in 1 second were observed. There was a significant decrease in mean diffusion capacity (diffusion lung capacity for carbon monoxide) (61.8±7.10 vs. 68.7±6.86\%) when compared with control ($P=0.000^*$).

\textbf{Introduction} Sexuality is considered as an important component of quality of life especially in those patients having chronic respiratory illness [1,2]. Female sexual dysfunction (FSD) is a complex disease attributed to several factors including physiological, psychological, medical problems, and social and culture environment. Absence or diminished sexual desire, problems in becoming aroused or lubricated, having an adequately stimulated orgasm, or presence of pain during intercourse were all associated disorders in FSD [3].

Interstitial lung diseases (ILDs) are a divergent group of chronic debilitating conditions resulting in progressive fibrosis of lung parenchyma, hence the chronic and progressive nature of the disease with burden of symptoms (e.g. progressive dyspnea, chronic cough, fatigue, anorexia, and malnutrition) and impaired gas exchange resulting in decrease physical activity and exercise tolerance. Though, the presence of the obstacles and sudden changes in lifestyle that affects sexual function and quality of life resulting in depression [4,5].

Sexuality is a topic that has rarely been studied in women with ILDs. The objective of the present study was to assess the sexual functioning and associated depressive symptoms in a sample of married women with ILDs.

\textbf{Patients and methods} This cross-sectional observational study was designed to measure female sexual function among women with ILDs. Data were collected from April 2017 to December 2017, Assiut University Hospital, Egypt. The study was accepted by the institutional ethics committees, and an oral approval from all patients was obtained.

A total of 65 participants were enrolled; 45 of them had ILD and fulfilled the inclusion criteria. The study population comprised 12 patients with idiopathic pulmonary fibrosis, 25 with connective tissue disease-associated interstitial pneumonias, and eight patients with other interstitial pneumonias. The
comparison group \((n=20)\) was age-matched women who were free of ILDs.

ILDs were diagnosed and classified according to recommended guidelines [6]. Diagnosis of ILDs was confirmed based on a review of the clinical history, pulmonary function test, and thin-section high-resolution computed tomography [6].

**Inclusion criteria**

All sexually active married female patients diagnosed as having ILDs were included.

**Exclusion criteria**

Pregnancy, lactation, menopause, previous history of hysterectomy, oophorectomy, or usage of oral contraceptive agents were the exclusion criteria.

All women were evaluated for the following:

1. **Full medical history**: age, BMI was calculated as body weight (kg)/height (m²), duration of disease, presence of comorbid disease, glucocorticoids as medication taken (dose and duration), and number of exacerbation within the past year.

2. **Pulmonary function tests**: all participants underwent resting pulmonary function tests including forced expiratory volume in 1 s and forced vital capacity (Zan 300; Sensor Medics MGA USB, Oberthulba, Germany) [7]. Diffusing capacity for carbon monoxide (DLCO) was measured (Zan 300; Sensor Medics MGA USB) according to the international guidelines [8].

3. **Hormonal profile**: blood samples for follicle-stimulating hormone (FSH) were collected at the follicular phase (3–7 days of menstrual cycle) and for estradiol and progesterone at the luteal phase (20–22 days of menstrual cycle). FSH levels in patients and controls were measured by enzyme-linked immunoassay test kits (Bio Check Inc., Vintage Park Dr., California, USA) using stat fax. The other hormones are estimated by enzyme-labeled chemiluminescent immunoassay using Immulite 1000 (catalog numbers are LKFS1, LKE21, and LKPW1).

4. **The female sexual function index (FSFI)**: the FSFI is a reliable questionnaire to measure sexual function, including six domains (desire, subjective arousal, lubrication, orgasm, satisfaction, pain) and 19 items for self-reported measurement. Each domain has a minimum and a maximum score (0–5), and the total score for sexual function is determined from all domains and has a maximum total score of 36. A score less than or equal to 26 has been validated as a cutoff score for diagnosing sexual dysfunction. Higher scores indicate better sexual functioning [9].

5. **Beck depression inventory (BDI)**: BDI is a self-report 21-inventory questionnaire to assess depression. Each question has a four-point scale to answer with respect to the intensity \((0–3)\), and the total score range is \(0–63\). BDI is accepted with a cutoff value greater than or equal to 17 for patients to have ‘depression’ [10].

**Statistical analysis**

Statistical analysis of collected data was determined using analysis of variance and Student’s \(t\)-test (SPSS version 16.0; SPSS Inc., Chicago, Illinois, USA) software for analysis. Results were expressed as mean \(±\)SD or number (percentage). Qualitative data were compared using either \(χ^2\)-test. \(P\) value less than 0.05 was considered significant.

**Results**

The baseline demographic data of study participants are presented in Table 1. The mean age of the ILD group \((n=45)\) was 40.4±8.9 years. A total of 15 (33.3%) patients of ILD group had systemic hypertension and 24 (53.3%) had pulmonary hypertension, whereas diabetes mellitus and dyslipidemia were found in

| Patients \((n=45)\) | Age (years) | BMI (kg/m²) | Having children | Systemic hypertension | Pulmonary hypertension | Diabetes mellitus | Dyslipidemia | Time since diagnosis of ILD (years) | Duration of glucocorticoids (years) | Dose of glucocorticoids (mg/day) | Exacerbation within last year |
|-------------------|-------------|-------------|-----------------|-----------------------|-----------------------|------------------|-------------|-----------------------------------|-----------------------------------|-------------------------------|-----------------------------|
|                   | 40.4±8.9    | 29.4±8.34   | 36 (80)         | 15 (33.3)             | 24 (53.3)            | 12 (26.6)       | 7 (15.5)    | 8.46±2.77                         | 9.23±2.31                         | 40.2±12.2                   | 2.3±0.8                     |

Values are expressed as mean±SD or number (%). ILD, interstitial lung disease. *Significant difference.
Table 2 Pulmonary function tests and hormonal assay level between both groups

| Test                  | ILDs group (n=45) | Control group (n=20) | P value |
|-----------------------|-------------------|----------------------|---------|
| DLCO%                 | 61.8±7.10         | 68.7±6.86            | 0.000*  |
| E2 (pg/ml)            | 34.2±8.4          | 47.0±9.8             | 0.000*  |
| FSH level (mIU/ml)    | 6.5±12.9          | 13.0±6.28            | 0.000*  |
| Progesterone level (nmol/L) | 13.06±6.28     | 38.32±9.77           | 0.000*  |

Data are expressed as mean±SD. DLCO, diffusion lung capacity for carbon monoxide; E2, estradiol; FEV1, forced expiratory volume in 1 s; FSH, follicle-stimulating hormone; FVC, forced vital capacity; ILD, interstitial lung disease. *Significant difference.

Table 3 Female sexual function index and Beck depression inventory scores in studied patients

| Test                          | ILDs group (n=45) | Control group (n=20) | P value |
|-------------------------------|-------------------|----------------------|---------|
| Total FSFI score             | 16.2±7.8          | 29.3±8.9             | 0.000*  |
| Prevalence of sexual disorder| 25 (55)           | 5 (25)               | 0.000*  |
| BDI score                    | 21.4±7.8          | 17.8±6.8             | 0.001*  |
| Prevalence of depression     | 36 (80)           | 7 (35)               | 0.001*  |

Values are expressed as mean±SD or number (%). BDI, Beck depression inventory; FSFI, female sexual function index; ILD, interstitial lung disease. *Significant difference.

26.6% and 15.5%, respectively. The mean duration since the diagnosis of ILD was 8.46±2.77 years, whereas the mean duration of using glucocorticoids was 9.23±2.31 years, with equivalent dose of 40.2±12.2 mg daily.

Regarding pulmonary function test, the present study revealed no significant differences were observed in forced vital capacity and forced expiratory volume in 1 s. In comparison with age-matched women without ILDs, significant decrease in mean value of DLCO has been reported (61.8±7.10 vs. 68.7±6.86%) (P<0.000*).

In relation to hormonal profile, increased in levels of FSH and lower progesterone level were demonstrated among ILD group (P=0.000*) (Table 2). Moreover, estradiol level was significantly decreased among ILD group as compared with control group.

Based on the results of the FSFI questionnaire within age-matched women with and without ILDs, we reported a higher prevalence of sexual dysfunction among married women with ILDs (55%). The mean FSFI total score was 16.2±7.8, which is significantly lower than those findings in control group (29.3±8.9). Furthermore, all the domains of female sexual function were affected: desire, arousal, lubrication, orgasm, global satisfaction, and pain (P=0.000*). Total FSFI scores and scores of each domain are shown in Table 3.

Our study demonstrated significant increase in the mean BDI scores (P=0.001*) and a higher distribution of women with depression among ILD group (80%), respectively (Table 3).

The relationship between age, BDI, and FSFI domains was investigated using Spearman’s correlation coefficient. Univariate analysis demonstrated that disease duration, duration of glucocorticoids and dosage (>20 mg), and depression were significantly associated with the FSFI total score (P<0.05). On the contrary, no significant relationships were found between FSFI global score age and BMI. A positive correlation was reported between DLCO and global FSFI scores (Tables 4 and 5).

Table 4 Domain scoring of female sexual function index in both groups

| Domain       | Item number | Score range | ILDs group (n=45) | Control (n=20) | P value |
|--------------|-------------|-------------|-------------------|----------------|---------|
| Desire       | 1, 2        | 1–5         | 3.26±1.8          | 4.58±1.19      | 0.000*  |
| Arousal      | 3, 4, 5, 6  | 0–5         | 2.73±1.11         | 3.23±2.15      | 0.000*  |
| Lubrication  | 7, 8, 9, 10 | 0–5         | 3.56±1.19         | 4.61±1.08      | 0.000*  |
| Orgasm       | 11, 12, 13  | 0–5         | 2.96±0.10         | 3.27±0.12      | 0.000*  |
| Satisfaction | 14, 15, 16  | 0 (or 1)–5  | 2.01±0.15         | 3.22±1.17      | 0.000*  |
| Pain         | 17, 18, 19  | 0–5         | 2.52±0.09         | 3.37±0.06      | 0.000*  |

Table 5 Correlation of the global female sexual function index score with sociodemographic variables, pulmonary function tests, and beck depression inventory score

| Variable       | Spearman’s r | P value |
|----------------|--------------|---------|
| Age (years)    | −0.233       | 0.341   |
| Duration of glucocorticoids | −0.452 | 0.000* |
| Dose of glucocorticoids (≥20 mg) | −0.400 | 0.002* |
| BMI            | −0.434       | 0.234   |
| BDI scores     | −0.086       | 0.000   |

BDI, Beck depression inventory scores; DLCO, diffusion lung capacity for carbon monoxide; r, correlation coefficient. P<0.05, significant.
Discussion

The effect of ILDs on female sexual function has not been well addressed. However, complexity and multifactorial nature of female sexual response adds to the difficulty in this point [11]. Thus, the purpose of our study was to spotlight and address the sexual dysfunction in women with ILD and quality of life.

Sexuality is known as the basic human right and a main component to achieve a healthy life. Hence, unhealthy sexuality contributes to physical and physiological burden which are attributed to ILDs place on female patients. Additionally, the presence of emotional burden may have a negative effect on sexual function and poor quality of life [1].

This study adds unique findings by using such a validated questionnaire, the FSFI, for the first time, to address women’s sexual function in ILDs. The FSFI is a reliable tool. It is considered not only as a standard reference in FSD evaluation but allows to identify specific dimensions of sexual function. Despite the peak reproductive period and sexual life in the studied group of women, we demonstrated a higher prevalence of sexual dysfunction in women with ILDs as compared with healthy age-matched group. Moreover, significant differences were found between both groups in all sexual dimensions: desire, arousal, orgasm, overall satisfaction, and dyspareunia. Several studies reported that sexual dysfunction is highly prevalent among patients with chronic pulmonary disease and had poor quality of life [4,12,13].

Likelihood, sexual dysfunction in patients with ILDs may be attributed to intimacy of many factors such as hormonal, physiological, psychological, or pharmaceutical factors. Reduction in exercise capacity secondary to hypoxemia, difficulty in breath, and general physical disability were all related to physiological factors, which not only hinder completion of sexual activity but also affect sexual desire and arousal, with an overall lower sense of satisfaction with their partner [14,15].

Furthermore, psychological factors concerning self-confidence, general depression, and anxiety about sexual performance; respiratory symptoms such as chronic cough; and poorer body image were all contributing factor [16].

Another important observation in our study was the association of sexual dysfunction and depressive symptom among women with ILDs. According to BDI questionnaire to evaluate depression, we demonstrated a higher prevalence of depression in ILD group when compared with control. Furthermore, a significant correlation was determined between BDI total score and global score of FSFI. In line with our results, Thombs et al. [17] reported that 65% of patients have clinically significant depression. Moreover, Roca et al. [18] observed that sexual dysfunction was closely associated with depression than any other functional domain. Thus, it is considered as a vicious cycle; an impaired sexual function was connected to more depression and worse quality of life.

Our study revealed that FSD was significantly correlated with disease duration and prolonged uses of glucocorticoid with high dose. Glucocorticoid may also affect women’s emotions. Thus, potential emotional adverse effects including depression, anxiousness, and irritability have negative effect on sexual function. In addition to emotional problems, steroids may cause water retention or bloating, resulting in poor body image and perceived attraction.

Hence, the interesting aspect explored in our study was increased prevalence of sexual dysfunction as determined with FSFI questionnaire and depressive symptom despite having mild impairment in their pulmonary function. These results were in agreement with previous studies who found that FSFI score and its domains were unrelated to disease classification and severity [19,20].

The high prevalence rates regarding sexual dysfunction existing among women with ILDs have reported, which may represent a significant concern and opportunity for education. Sexual dysfunction identifies a key area for clinicians to proactively engage their patients in open discussion about sexual health and the available treatment options [21,22].

Recently, flibanserin is the first FDA-approved medication options to assist women affected by FSD. Flibanserin focuses on the role of neurotransmitters within the sexual response. It acts as a serotonin 5-HT1A agonist in addition to a 5-HT2A antagonist. Despite, flibanserin having reported efficacy with increased total FSFI and desire domain scores in several clinical studies for better sexual life, it is still in need for additional study in associated medical condition such as chronic pulmonary disorders [23].

In conclusion, ILDs have unfavorable effects on the quality of sexual function of female patients leading to...
impaired sexual life and more depressive symptoms. However, such a problem has not been given the attention it warrants. Sexual problems are often neglected during assessment and evaluation of patients with ILDs. In fact, good sexual function is important for a better quality of life.

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Conflicts of interest
There are no conflicts of interest.

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