

## Sexual Dysfunction in Women Being Treated with SSRIs

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**Abstract:** Selective Serotonin Reuptake Inhibitors (SSRIs) are the most commonly prescribed drugs for depression and anxiety disorders. We aimed to evaluate treatment-emergent sexual dysfunction (SD) in 100 women who were diagnosed with depression and anxiety disorders and on treatment with SSRIs. Hamilton Depression Rating Scale and Hamilton Anxiety Rating Scale were applied to identify women in remission. Changes in sexual functioning questionnaire-Female version (CSFQ-F-C) was applied to measure SD. Women on SSRIs for depressive and anxiety disorders had high rates of global and phase-specific SD. 28% of the participants experienced global SD and 74% of the participants experienced phase-specific SD in at least one of the domains. 70% of patients experienced reduced sexual pleasure, 56% of patients experienced reduced sexual interest, 53% of patients experienced reduced sexual excitement, 53% of patients experienced reduced orgasm and 48% of patients experienced reduced sexual desire/frequency. Our study highlights the importance of evaluating SD using validated scales in routine clinical care which otherwise may go unaddressed.

**Keywords:** SSRIs, CSFQ, Sexual dysfunction, Depression, Anxiety.

### INTRODUCTION

Depression and anxiety disorders are two of the leading causes of disease burden worldwide [1]. Antidepressant medications are the most common treatment for these disorders and among the antidepressants 60% receive Selective Serotonin Reuptake Inhibitors (SSRIs) or Serotonin Norepinephrine Reuptake Inhibitors (SNRIs) [2].

Research has shown that there is a bidirectional association between depression and sexual dysfunction (SD). Depression leads to a 50-70% increased risk of SD as reported by Atlantis and Sullivan in a review and meta-analysis [3].

Antidepressants are known to be some of the most common medications which negatively impact the sexual functioning of individuals [4]. Changes in sexual functioning questionnaire (CSFQ) developed by Clayton *et al.* [5] and the Arizona Sexual Experience Scale (ASEX) developed by McGahuey *et al.* [6] are primary validated scales used to assess SD [4,7]. Rothschild reviewed research looking at antidepressant associated SD and concluded that 40% of people on antidepressants would experience some form of SD [8]. A meta-analysis done in 2009 revealed that citalopram, escitalopram, fluoxetine, fluvoxamine,

paroxetine, sertraline, duloxetine, venlafaxine, imipramine, and phenelzine were associated with significantly higher rates of SD compared with placebo and with absolute values of SD ranging from 25% to 80% of patients [9]. About 5-10% of patients will experience spontaneous reduction in SD after being on antidepressant for 4-6 months but the rest continue to experience SD despite remission in depressive symptoms [10].

Desire, arousal and orgasm are the 3 phases of sexual cycle. Animal studies have shown that preoptic area plays a role in sexual motivation, ventromedial nucleus for sexual receptivity and paraventricular for arousal. Prolactin and serotonin presumably by inhibition of dopamine reduce motivation or desire, serotonin reduces arousal and descending serotonin pathways via 5HT<sub>2A</sub>, 5HT<sub>2C</sub> reduces orgasm.

Anticholinergic action of SSRIs cause erectile dysfunction by its anticholinergic action and it also stimulates 5HT<sub>2A</sub> in the mesocortical pleasure centres which may reduce dopamine activity leading to reduced libido [11,12].

Women are 2½ times more likely to be put on antidepressant medications than men [13]. Reports have suggested high rates of female SD with antidepressants. Prevalence with various classes of antidepressants is as follows- Tricyclic antidepressants- 30%, SSRIs- 25-75% and SNRIs- 58-70% [9,14]. Decreased excitement, reduced libido and delayed orgasms were the most frequently reported problems [9,15].

A study done in 2012 on Indian population revealed that 42.5% of patients on SSRIs for depression had SD. In that study 95% had decreased desire, 60% had decreased arousal, 37.5% had decreased lubrication, 63.8 had decreased orgasm, 55% had decreased satisfaction and 25% had pain during sexual activity [16]. SD can have significant impact on the person's quality of life [17], quality of relationships, self esteem, recovery and can even lead to non-compliance with antidepressant treatment with a potential for relapse of symptoms [18]. Studies have shown that patients with SD have greater adherence to negative stereotypes about pharmacological therapy and this is especially true in women with SD who reported significant negative impact on all areas of quality of life.

There are various strategies to manage the SD associated with SSRIs which include switching to a different group, reducing the dose, drug holidays, adding an antidote or wait for spontaneous remission (adaptation). As risk of relapse is high when reducing the dose and drug holidays may encourage patients to be non compliant, the most commonly used treatment is augmentation (Bupropion or Bupirone) or addition of an antidote (PDE-5 inhibitors) which ameliorate the symptoms [14,19].

Our research is relevant as literature on SSRI induced female sexual dysfunction in Indian population is scant. In addition, evaluation of sexual functioning in females with depression and anxiety disorders is important as it may have a significant impact on quality of life. The objectives of the study were- to estimate the prevalence of sexual dysfunction in women on treatment with SSRIs for anxiety and depressive disorders; and to study the association between various socio-demographic and clinical variables with sexual dysfunction.

## MATERIALS AND METHODS

### Study design

This was an observational, cross-sectional survey using purposive sampling conducted in Department of Psychiatry, Yenepoya medical college

hospital, Mangalore, Karnataka, India which is a tertiary care teaching hospital. Ethical clearance was obtained from the institutional ethics committee.

### Study sample

100 female patients attending the outpatient department or admitted in the ward and who were on antidepressants for a minimum period of 2 weeks were included in the study. Female patients who were married, not attained menopause and on SSRIs for an ICD-10 diagnosis of depression (first episode depression or recurrent depressive disorder) or anxiety disorder were approached to participate in the study. Patients on multiple antidepressants and on other psychotropics except benzodiazepines were excluded from the study. Participants with other comorbid psychiatric/neurologic disorders and those with sexual dysfunction prior to their diagnosis of depressive/anxiety disorder were excluded.

### Procedures

Patients who gave written informed consent were evaluated with Hamilton Depression Rating Scale (HAM-D) and Hamilton Anxiety Rating Scale (HAM-A) to ascertain remission of symptoms (HAM-D score less than 7 and HAM-A score less than 14). Subjects were informed that they would be assessed for presence of sexual dysfunction using "Changes in sexual functioning questionnaire-Female Clinical version (CSFQ-F-C)" and they were free to opt for its treatment or refuse.

### Measures used

CSFQ-F-C is an extensive questionnaire which evaluates every stage of sexual functioning in females. It is a self-report questionnaire with 14 questions answered on a likert scale of 1-5. The questionnaire gives total and various sub-scale scores corresponding to each stage of sexual cycle. The Desire phase of the sexual response cycle is measured by five items to assess frequency and interest in participating in sexual activity. The Arousal phase is measured by three items to assess excitement and physical changes related to arousal (e.g., vaginal lubrication, functional erections). The Orgasm phase is measured by three items to assess the respondent's ability to achieve orgasm and related pleasure. Three additional items are included in the overall measure of global functioning: pleasure from sexual activity, loss of interest after arousal (women)/prolonged erections (men) and pain associated with orgasm. Because the score for global sexual dysfunction includes these three items not included on any phase scale, it is possible to have dysfunction in all three phases of the sexual response cycle without meeting total CSFQ score criteria for global sexual dysfunction [5]. Cut-off scores are provided for total and sub-scale scores. Scores at or below cut-off points are indicative of sexual dysfunction. The internal consistency and convergent validity of CSFQ-14 is found to be modest to good in previous studies [7].

Hamilton Anxiety Rating Scale (HAM-A) is a clinician rated scale with 14 items each rated on a likert scale of 0 (not present) to 4 (severe). The total score range is 0-56 and a score of less than 14 indicates remission of anxiety symptoms [20]. The reliability and concurrent validity were found to be acceptable in studies [21,22].

Hamilton Depression Rating Scale (HAM-D) is a clinician administered scale with 17 items rated on a likert scale of 0-2 or 0-4 in case of certain items. The total score range is 0- 52 and a score of less than 7 indicates remission of depression [23]. The scale’s internal reliability is adequate but content validity is poor; convergent validity and discriminant validity are adequate [24].

Statistical analysis: The discrete variables were presented as percentages/proportions. Continuous variables were expressed in terms of mean and standard deviation. Chi-square tests were performed to study association between categorical variables. Pearson bivariate correlation was done to study relationship between age, dosage of antidepressants and sexual dysfunction.

**RESULTS**

Socio-demographic characteristics of sample: Mean age of the sample was 34.98±6.98 years. More than half (53%) of the participants followed Hindu religion and 46% belonged to Muslim religion. 73% of the participants belonged to low and middle socio-economic class and 27% belonged to high socio-economic class. 63% of the sample were educated up to primary school and 37% had high-school education or higher (Table 1).

**Table-1: Socio-demographic characteristics of sample**

<b>Age</b>	<b>Mean- 34.98, SD-6.98</b>
<b>Religion</b>	<b>n (%)</b>
Hindu	53 (53%)
Muslim	46 (46%)
Christian	1 (1%)
<b>Socioeconomic Status</b>	<b>n (%)</b>
Low and Middle	73 (73%)
High	27 (27%)
<b>Education</b>	<b>n (%)</b>
Up to Primary school	63 (63%)
High school & Above	37 (37%)

Clinical characteristics of the sample: Majority of the participants were diagnosed with Depressive disorder (78%) and rest of the patients had received a diagnosis of Anxiety Disorder (22%). Majority of the sample were on Escitalopram (75%) and a quarter of the subjects were receiving Sertraline (25%). The mean dosage of Escitalopram was 11.93 (±3.72) mg and that of Sertraline was 84 (±23.80) mg. Patients were on treatment with antidepressants for a mean duration of 10.3 (±11.76) months with a range of 1-72 months (Table 2).

Sexual dysfunction in the participants: 28% of the participants had CSFQ-F-C score less than cut-off which implies that they experienced global sexual

dysfunction impacting all the phases of the sexual response cycle. Three fourth of the participants experienced dysfunction in at least one of the phases of sexual response cycle. 70% of patients experienced reduced sexual pleasure (Mean CSFQ-subscale score- 3.75, Cut-off- 4); 56% of patients experienced reduced sexual interest (Mean CSFQ- subscale score- 8.92, Cut-off- 9); 53% of patients experienced reduced sexual excitement (Mean CSFQ-subscale score- 11.31, Cut-off- 12); 53% of patients experienced reduced orgasm (Mean CSFQ-subscale score- 10.39, Cut-off- 11) and 48% of patients experienced reduced sexual desire/frequency (Mean CSFQ-subscale score- 6.73, Cut-off- 6) (Table 2).

Tabl-2: Clinical characteristics of the sample

<b>Diagnosis</b>	
Depressive disorder	78 (78%)
Anxiety disorder	22 (22%)
<b>SSRI used for treatment</b>	
Escitalopram	75 (75%)
Sertraline	25 (25%)
<b>Dosage of SSRI</b>	
Escitalopram	Mean- 11.93 mg, SD- 3.72 mg
Sertraline	Mean- 84 mg, SD- 23.80 mg
<b>Duration on SSRI</b>	Mean- 10.3 months, SD- 11.6 months
<b>Sexual dysfunction</b>	
Global sexual dysfunction	28 (28%)
Reduced sexual pleasure	70 (70%)
Reduced sexual interest	56 (56%)
Reduced sexual excitement	53 (53%)
Reduced orgasm	53 (53%)
Reduced sexual desire/frequency	48 (48%)

### Relationship between education, socio-economic status and sexual dysfunction

Chi-square tests were performed to study the relationship between socio-demographic variables such as educational and socio-economic status with global sexual dysfunction which revealed that there was no statistically significant association between them.

### Correlation between age and sexual dysfunction

A Pearson product-moment correlation coefficient was computed to assess the relationship between age of the participants and global sexual dysfunction (total CSFQ score). There was a weak positive correlation between the two variables,  $r= 0.30$ ,  $n= 100$ ,  $p= <0.001^{**}$ .

### Correlation between dosage of SSRI and sexual dysfunction

A Pearson product-moment correlation coefficient was computed to assess the relationship between dosage of escitalopram and global sexual dysfunction (total CSFQ score). There was a negligible positive correlation between the two variables,  $r= 0.09$ ,  $n= 75$ ,  $p= 0.008^*$ . A Pearson product-moment correlation coefficient was computed to assess the relationship between dosage of sertraline and global sexual dysfunction (total CSFQ score). There was no significant correlation between the two variables,  $r= 0.02$ ,  $n= 25$ ,  $p= 0.41$ .

## DISCUSSION

Women on SSRI monotherapy had high rates of global and phase-specific sexual dysfunction. 28% of the participants in this study experienced global sexual dysfunction and 74% of the participants experienced phase-specific sexual dysfunction in at least one of domains. In addition to the 28% of women who experienced global dysfunction, 70% of women

experienced reduced sexual pleasure, 56% of women experienced reduced sexual interest, 53% of women experienced reduced sexual excitement, 53% of women experienced reduced orgasm and 48% of women experienced reduced sexual desire/frequency. Most studies which have evaluated treatment emergent sexual dysfunction have included participants of both gender irrespective of their marital status and have not evaluated for the presence of psychopathology and other medications which may influence the results. In the current study the participants had complete remission of symptoms and were not on any other medication except on either of the two SSRIs (Escitalopram and Sertraline). There was no association between socio-demographic variables like education and socio-economic status with SD. Although there was a positive correlation between age and SD, the effect size was small indicating a weak correlation. Thus, confounding of the results by age-associated SD, depression, anxiety and other drugs causing sexual dysfunction were excluded.

A meta-analysis was done by Serretti and Chiesa [9] in 2009 to quantify sexual dysfunction associated with antidepressants which included studies specifically evaluating sexual functioning using validated questionnaires. The analyses revealed that significantly higher rate of total treatment-emergent SD and specific phases of dysfunction compared with placebo for the following drugs in decreasing disorder-sertraline, venlafaxine, citalopram, paroxetine, fluoxetine, imipramine, phenelzine, duloxetine, escitalopram and fluvoxamine. The rates of sexual dysfunction ranged from 25.8% to 80.3% [9]. Other studies have reported a prevalence of treatment-emergent sexual dysfunction in the range of 40—70% for SSRIs such as citalopram, escitalopram, paroxetine and fluoxetine which is higher than noted in

our study [10,25-33]. A report from India which evaluated married women diagnosed with depression and on SSRIs concluded that 43.63% of participants experienced SD [16].

In a study by Clayton *et al.* [15] which looked at phase-specific SD caused by SSRIs reported that 95.6% of the female participants reported SD in at least one of the domains. Another study from India which looked at antidepressant associated SD in married females diagnosed with depression reported that 95% of the sample had SD in at least one of the domains [16]. These rates are higher than found in our study in which 74% of the participants reported SD in at least one of the domains.

A meta-analysis done in 2009 which attempted to quantify the phase-specific SD associated with various SSRIs concluded that arousal dysfunction (82-84%) was the most commonly affected domain followed by desire dysfunction (71-74%) and orgasm dysfunction (39.5- 45%) [9]. A study by Grover *et al.* [16] revealed that among women on SSRIs 91% had decreased desire followed by 65.45% with orgasmic dysfunction and 60% with arousal dysfunction. These reports are in contrast with our findings which concluded that sexual pleasure was the most commonly affected domain. The rates of desire dysfunction (48%), arousal dysfunction (53%) and orgasmic dysfunction (53%) seen in our sample were much lower compared to previous studies.

The lower rates of global and phase-specific SD in our sample may be due to under-reporting as it is a taboo to discuss sexual life in India, especially in women. In addition, the participants in this study were mostly on escitalopram (75%) which has been shown to be associated with lower rates of SD among the SSRIs whereas most of the previous studies had other antidepressants including other SSRIs and SNRIs. The differences may be explained by the fact that previous studies used a variety of rating scales to measure SD which may lead to heterogeneous results.

The study had a cross-sectional design and used purposive sampling. Subjects were women seeking treatment for anxiety and depressive disorders from a tertiary care hospital and may not be representative of the general population. Pre-treatment rates of sexual dysfunction were not available for the study sample. There was no control group in this study and a literature review did not provide rates of sexual dysfunction in the population. The study did not assess compliance of the subjects to the antidepressants. Majority of the participants were on escitalopram and other few were on sertraline. The results of this study should be seen in the light of these limitations and a causal linkage between antidepressant use and sexual dysfunction cannot be made.

Despite the limitations, this was one of the few studies from southern parts of India which throws light on sexual dysfunction in women being treated with SSRIs. We used a validated measure to assess sexual dysfunction and participants who had sexual dysfunction prior to the onset of depression or anxiety disorder were excluded. In addition, participants who were still symptomatic were excluded which reduced the chances of confounding due to presence of psychopathology. Future research with prospective design, larger sample size, including controls and patients on other classes of antidepressants should overcome these limitations.

## CONCLUSION

Women on treatment with SSRIs frequently experience sexual dysfunction. Majority of the women experience dysfunction in at least one of the phases of the sexual response cycle if not global dysfunction. Our study highlights the need for assessment of sexual functioning using validated rating scales in all patients on SSRIs rather than relying on spontaneous reporting.

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