



Predictors of Sexual Dysfunction in Women Seeking Treatment for Opioid Use Disorder: A Comparative Cross-Sectional Study from a Tertiary Center

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Abstract

Aim: There is a critical need for scientific evidence on the sexual and reproductive health of women with opioid use disorder (OUD). The main objective of this study was to evaluate sexual dysfunction (SD) and depression in women with OUD and compare them with healthy controls, in addition to exploring possible predictors of SD.

Methods: This cross-sectional study was conducted between January and July 2023. Thirty-four women with OUD, according to the DSM-5, and 30 healthy controls were included. The Female Sexual Function Index (FSFI), Patient Health Questionnaire-9 (PHQ-9), and sociodemographic questionnaire were used to evaluate SD, depression, and characteristics related to substance use and sexual/reproductive history. Logistic regression analysis was performed to determine the predictors of SD in women with OUD.

Results: Twenty-nine percent (n=10) of the participants with OUD had SD. The scores of the FSFI desire, arousal, lubrication, orgasm (p=0.001 for all), satisfaction (p=0.001) subscales, and the total score (p<0.001) were lower in women with OUD than in the controls. Daily dosage of buprenorphine/naloxone [Odds ratio (OR)=1,956, p=0.027, 95% confidence interval (CI)=1,079-3,545] and PHQ-9 score (OR=1,403, p=0.012, 95% CI=1,076-1,829) were significantly associated with SD in women with OUD.

Conclusion: The high prevalence of SDs highlights the unmet sexual health needs of women with OUD. Screening and addressing depressive symptoms should be one of the first steps when caring for SDs in women with OUD.

Keywords: Opioid use disorder, sexual dysfunction, depression, female, buprenorphine/naloxone drug combination

Introduction

Opioid use disorder (OUD) is a chronic, relapsing condition that necessitates long-term treatment, particularly pharmacological management [opioid maintenance treatment (OMT)] combined with psychosocial interventions. OMTs include methadone (mu-opioid receptor agonist) and buprenorphine (bup) (a partial mu (μ) receptor agonist). Bup is the only OMT legally available in Turkey and can be prescribed as a bup/naloxone (nal) combination for the maintenance treatment of OUD. Maintenance of abstinence is a major

issue in OUD, and the adverse effects of OMTs can disrupt treatment compliance.

Opioids, both endogenous and exogenous, both as a substance for abuse or for therapeutic purposes (such as in bup/nal), may influence the endocrine system (1) and have a role in sexual functioning (2). They have been demonstrated to cause hypogonadism by disrupting the hypothalamic-pituitary-adrenal axis, leading to a decrease in libido and erectile dysfunction in men (1,3). Additionally, they might also have an impact on the entire sexual cycle. The majority of research on alterations in



sexual functioning was collected from male participants with OUD and/or OMT (4-6). A meta-analytic study of men with OUD revealed that the prevalence of sexual dysfunction in those taking methadone was 52%, almost twice that of those taking buprenorphine (24%), which is still highly prevalent (7). Despite the more severe medical, psychiatric, and functional consequences associated with substance use disorders (SUDs) in women, there is still very little research on sexual dysfunctions in women with OUD (8).

In addition to sexual health concerns, poor reproductive outcomes, such as an increased risk of contracting and transmitting sexually transmitted infections, a higher prevalence of unintended pregnancies, and a lower amount of contraceptive use, are frequently presented among women with SUDs (9-12). Reproductive and sexual health are essential parts of human well-being and interrelatedly affect each other. Additionally, psychiatric and social conditions may further complicate the reproductive and sexual outcomes of women with OUD (11). Therefore, collaborative management and implications of reproductive and sexual health interventions with OMTs may be beneficial (13).

Depression is the most common psychiatric comorbidity associated with OUD and has a bidirectional relationship with sexual dysfunction (14,15). Research has indicated that a large number of women with depression, ranging from 70% to 80%, may suffer from sexual dysfunction (16). On the other hand, the lifetime prevalence of depression in people with OUD could be up to 75% (14). The link between SD and depression in OUD could be due to comorbidities (psychiatric disorders, other treatments, etc.) and conditions (low socioeconomic status, traumatic experiences, etc.) associated with OUD (17). Furthermore, long-term OMT may lead to opioid-induced hypogonadotropic hypogonadism, which can impair androgen production and thus affect sexual function in women with OUD (17). However, there is still a lack of clarity.

There is a critical need for scientific evidence to identify practice gaps and guide planning and action to meet the sexual and reproductive health needs of women with OUD. The objective of this study was to examine and evaluate sexual dysfunction and depressive symptomatology in women seeking treatment for OUD and to compare it with a healthy control group in a Turkish sample. Our second aim was to explore the predictors and clinical correlates of sexual dysfunction in women with OUD. In addition, we investigated the characteristics related to the reproductive health of treatment-seeking women with OUD.

Methods

Compliance with Ethical Standards

The study was approved by the Clinical Research Ethics Committee of University of Health Sciences Turkey, Erenkoy Training and Research Hospital for Psychiatry and Neurological Diseases (date: 07.04.2023, approval no: 26) and executed in compliance with the regulations set forth in the Declaration of Helsinki and International Conference on Harmonization/Good Clinical Practice guidelines. Written informed consent was obtained from all participants before they enrolled in the study.

Study Design

This single-center, cross-sectional study included 34 treatment-seeking individuals with a diagnosis of OUD according to the Diagnostic and Statistical Manual of Mental Disorders-5 (DSM-5), who had applied for inpatient, outpatient, and rehabilitation clinics in the Alcohol and Substance Use Research, Treatment, and Education Center of Erenkoy Training and Research Hospital for Psychiatry and Neurological Diseases. This specialized unit is a referral center for primary and secondary healthcare services and admits patients from a broad geographical region, including urban and rural areas. The diagnosis of participants was confirmed by mental health professionals (M.E. and M.K.K.) who have expertise in addiction medicine. The participants were enrolled in the study consecutively between January and July 2023. Participants were included if they were 1) a woman aged 18-65 years, 2) diagnosed with OUD according to, and 3) sexually active during the last four weeks. Because no women with OUD within the inclusion criteria were hospitalized on the specified dates of our study, only outpatient participants were included. The exclusion criteria were as follows: 1) illiteracy; 2) being under the influence of any substance or alcohol or exhibiting withdrawal symptoms; 3) previous or current psychosis, intellectual disability, bipolar disorder, organic mental disorder, or dementia; 4) severe vital organ dysfunction; 5) being pregnant, in the postpartum period, on lactation, or on menopause; 6) the presence of a previously diagnosed neurological, metabolic, or endocrinological disorder. Before starting the study, six patients were excluded due to not being sexually active during the last four weeks, one for menopause, and two for not fulfilling the self-report scales (Figure 1). The control group comprised individuals who had attended the routine medical board report to apply for a job, as well as medical staff, their family members, and students. A sociodemographic and clinical data form, the Patient Health Questionnaire-9 (PHQ-9), and the Female Sexual Function Index (FSFI) were used for the analysis.

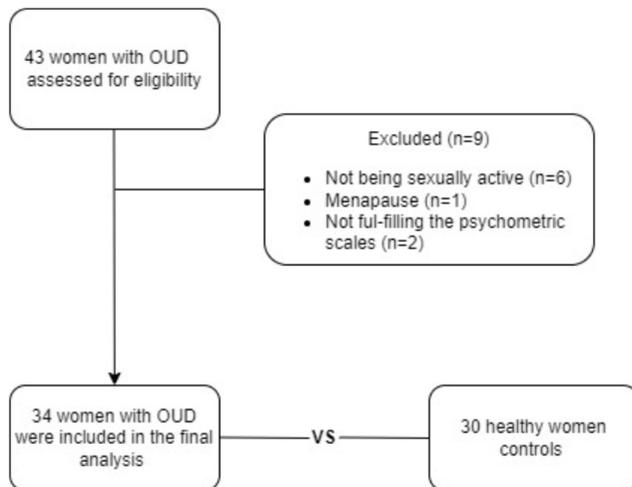


Figure 1. Study flow chart
 OUD: Opioid use disorder

Sociodemographic and Clinical Data Form

The sociodemographic data form designed by the researchers contained information about the participants' demographic data, characteristics related to substance use, and brief sexual and reproductive histories. Height (cm) and weight (kg) with light clothing were measured. Body mass index [weight (kg)/height² (m²)] was calculated to assess relative body fatness. Those with a menstrual cycle of 21-45 days were considered regular, while others were presumed to have an irregular menstrual cycle, and those without a menstrual period for 3 consecutive months were considered amenorrheic (18). Birth control planning methods were considered effective if the contraception method was one of the following: oral contraceptive pills, estrogen-progestin patches, condoms, diaphragms, or intrauterine devices.

Patient Health Questionnaire-9

The PHQ-9 depression module was employed to measure depressive symptoms. The PHQ-9 is a reliable and valid self-report tool for clinical and research use that evaluates the DSM criteria of depression from 0 (not at all) to 3 (nearly every day), producing a severity score ranging from 0 to 27 (19). A score of 5, 10, 15, or 20 corresponds to mild, moderate, moderately severe, and severe depression, respectively. PHQ-9 was found to be a valid and reliable screening tool for people with SUD (20).

Female Sexual Function Index

The FSFI was used to assess sexual functions over the last four weeks. This self-report scale consists of 19 items and 6 domains: desire, arousal, lubrication, orgasm, satisfaction, and pain (21). The first two items are rated on a five-point Likert scale (1 to 5), and the other items are rated on a six-point scale (0-6). The total score of the

scale ranges between 2 and 36, and higher scores indicate better sexual functioning. A study on the reliability and validity of the Turkish version was conducted by Aygin (22) and demonstrated an internal consistency coefficient ranging between 0.70 and 0.96. The established cut-off for a diagnosis of sexual dysfunction in women across ages (18-74 years) and lifestyles is ≤ 26.55 for the total score (23).

Statistical Analysis

All statistical analyses were conducted using SPSS (Statistical Package for Social Science) version 21.0 software (IBM SPSS Statistics, New York, United States). The Kolmogorov-Smirnov test was performed to test normality. Non-normally distributed data are presented as medians and interquartile ranges (25th percentile and 75th percentile). Since the continuous variables did not follow a normal distribution, the Mann-Whitney U test was used to compare the characteristics of the OUD and control groups. Numbers and percentages are provided for the categorical data. The chi-square test was used to compare categorical variables. A binary logistic regression analysis was performed on the possible factors identified using univariate analyses to determine the predictors of sexual dysfunction in women with OUD. The presence of sexual dysfunction was defined according to the FSFI cutoff score. The Hosmer-Lemeshow test indicated that the model fits the data well [χ^2 (8)=8,204, $p=0.414$]. The likelihood ratio test [χ^2 (2)=18,716, $p<0.001$] demonstrated that the logistic model was more effective than the intercept-only model. The level of significance was set at $p<0.05$ for all analyses.

Results

The socio-demographic, reproductive, and sexual history characteristics of OUD and control participants are presented in Table 1. Thirty-four women with OUD and thirty controls were recruited for the study. There was no statistical difference between the control and OUD groups in terms of age ($p=0.083$). Years of education, being employed or a student, and being married were statistically significantly higher in the control group ($p=0.001$, $p<0.001$, $p<0.001$, respectively). The control group employed effective contraception more frequently ($p=0.007$), whereas women with OUD had more abortion histories ($p=0.042$) and a greater number of sexual partners in the last year ($p=0.011$).

FSFI scores among the OUD and control groups revealed significant differences in desire, arousal, lubrication, orgasm, satisfaction, and total score, indicating worse sexual functionality in women with OUD (Table 2). The pain subscale of FSFI did not differ between the two groups ($p=0.196$). Patients with OUD had significantly

Table 1. Socio-demographic, reproductive, and sexual history characteristics of participants

	OUD (n=34)	Controls (n=30)	Statistics
Age	25.5 (24-37)	29 (27-36)	p=0.083
Education (in years)	12 (8-13)	15 (13-15)	p=0.001
Occupational status -Employed/student -Unemployed	13 (38.2%) 21 (61.8%)	29 (96.7%) 1 (3.3%)	p<0.001
Marital status -Single -Married	23 (67.6%) 11 (32.4%)	6 (20%) 24 (80%)	p<0.001
Having children (yes)	12 (37.5)	13 (43.3%)	p=0.640
BMI (kg/m ²)	21.16 (19.81-25)	23.09 (20.6-25.8)	p=0.102
Menstrual cycle -Regular -Irregular -Amenorrhea	27 (79.4%) 2 (5.9%) 5 (14.7%)	28 (93.3%) 2 (6.7%) 0	p=0.091
Sexual orientation -Heterosexual -Homosexual -Other	32 (100%)	30 (100%)	-
Birth control method -Effective (yes) -Condom -Oral contraceptive -Penile withdrawal before ejaculation -Intrauterine device -None	8 (23.5%) 4 (11.8%) 3 (8.8%) 4 (11.8%) 1 (2.9%) 22 (64.7%)	17 (56.7%) 10 (33.3%) 3 (10%) 3 (10%) 4 (13.3%) 10 (33.3%)	p=0.007*
No. of pregnancies	1 (0-1)	0 (0-1)	p=0.835
No. of deliveries	0 (0-1)	0 (0-1)	p=0.778
No. of abortions	0 (0-1)	0 (0-0)	p=0.042
No. of sexual partners in last year	1 (1-2)	1 (1-1)	p=0.011
Sexual activity while intoxicated -Last year (Yes) -Life-long (Yes)	8 (23.5%) 24 (70.6%)	0 0	p=0.005 p<0.001
Exchanged sex for money/substance -Last year (yes) -Life-long (yes)	2 (5.9%) 3 (8.8%)	0 0	p=0.177 p=0.096

*Effective vs. ineffective/none, OUD: Opioid use disorder
Mann-Whitney U and chi-squared tests were performed

Table 2. Psychometric scale scores among comparison groups

	OUD	Controls	Statistics
Desire	3 (1.8-4.2)	4.2 (3.6-4.8)	p<0.001
Arousal	3 (1.8-3.9)	4.8 (3.9-5.1)	p<0.001
Lubrication	3.75 (2.7-4.5)	5.25 (4.5-6)	p<0.001
Orgasm	3.6 (2.4-4.8)	5 (4.8-5.6)	p<0.001
Satisfaction	4.4 (2.4-5.2)	5.2 (4.8-5.6)	p=0.001
Pain	4.6 (3.6-5.6)	5.2 (4.4-5.8)	p=0.196
Total-FSFI	22.35 (16.5-26.7)	29.75 (27.8-31.3)	p<0.001
PHQ-9	12.5 (10-19)	5 (4-9)	p<0.001

OUD: Opioid use disorder, FSFI: Female sexual function index, PHQ-9: Patient health questionnaire-9. Mann-Whitney U test was performed

higher scores on the PHQ-9 than controls (p<0.001). Of the OUD group, 76.5% (n=26) had moderate to severe depression, whereas this rate was 20% in the controls.

29.4% (n=10) of the participants with OUD had sexual dysfunction, according to the FSFI. There was no statistically significant difference in the age at onset of substance use (p=0.956), age at onset of opioid use (p=0.752), duration of opioid use (p=0.752), history of inpatient treatment for OUD (p=0.452), or presence of intravenous administration of opioids (p=0.961) between women with and without sexual dysfunction in the OUD group. The daily dosage of bup/nal treatment (p=0.042) and the total score of PHQ-9 (p=0.003) were significantly higher in the group with sexual dysfunction. Characteristics related to substance use and depression in the OUD group according to the presence of sexual dysfunction are summarized in Table 3.

Logistic regression analysis revealed that the daily dosage of bup/nal treatment (OR=1,956, p=0.027, 95% CI=1,079-3,545) and total PHQ-9 score (OR=1,403, p=0.012, 95% CI=1,076-1,829) were significantly associated with the presence of sexual dysfunction in women with OUD. Table 4 demonstrates the results of the logistic regression.

Discussion

The aim of the present study was to explore sexual dysfunctions, depressive symptomatology, and characteristics related to reproductive health in women with OUD and to compare them with a healthy control group, in addition to investigating predictors and clinical correlates of sexual dysfunction in women with OUD. Our results revealed that almost a third of the women with OUD had been experiencing sexual dysfunction, differing significantly from the healthy controls in all domains of sexual functioning except for pain. Depression, along with the daily dosage of bup/nal treatment, predicted sexual dysfunction in women with OUD. It was established that women with OUD had inadequate resources regarding reproductive health (utilizing ineffective birth control methods and higher abortion rates) and exhibited risky sexual behaviors (engaging in sexual activity while intoxicated).

Despite the greater prevalence of UOD in men, the gender gap has been narrowing, indicating a critical need for study in women with OUD. A 2022 study conducted in Turkey revealed that 7.6% of those who declared that they had used heroin at any point in their lives were women

(24). Women with SUDs tend to demonstrate a higher degree of impairment in terms of employment, social/family functioning, and medical functioning compared with men, as well as worse psychiatric outcomes (8). Due to the high level of burden associated with OUD in women, every effort to improve quality of life and treatment compliance, including assessment and intervention for sexual dysfunctions, is critical.

Studies on men with bup/nal treatment due to OUD demonstrated significant sexual dysfunctions such as erectile dysfunction (25,26), loss or reduction in sexual desire, and ejaculatory problems. A 4-month follow-up study in men with OUD revealed that bup/nal treatment resulted in an increase in sexual problems (6). Our research revealed a significant decrease in almost all domains of sexual functioning in women with OUD compared with controls. In line with our findings, a limited number of other studies have shown worse sexual functioning in women with OUD (17,27). It is likely that the widespread sexual dysfunction experienced by women with OUD is the result of a variety of biological, medical, psychological, sociocultural, political, economic, and interpersonal factors, thus demonstrating the complexity of the relationship between sexuality and OUD. Despite the high rates of sexual dysfunction in OUD, help-seeking behavior was observed to be very low in previous research, underpinning the need for proactive inquiry about the sexual health of patients (28).

Opioids, serotonin, and endocannabinoids are key neuromodulators of inhibitory pathways in the female sexual response cycle; thus, OUD and OMT may have a

Table 3. Characteristics related to substance use and depression in OUD group according to presence of sexual dysfunction

	SD+ (n=10)	SD- (n=24)	Total (n=34)	Statistics
Age at onset of substance use	17.5 (15.5-22)	19 (16-21)	18 (16-22)	p=0.956
Age at first opioid use	18 (17-22.5)	20 (18-21)	18.5 (17-22)	p=0.752
Duration of opioid use (months)	60 (36-90)	66 (36-108)	60 (36-96)	p=0.752
IV usage (yes)	7 (27.3%)	3 (30%)	10 (29.4%)	p=0.961
Daily dosage of Bup/Nal treatment	10 (8-14)	9 (4-10)	10 (8-12)	p=0.042
History of inpatient treatment for OUD (yes)	13 (54.2%)	4 (40%)	17 (50%)	p=0.452
PHQ-9	15.5 (12-19)	9 (5-11)	12.5 (10-19)	p=0.003
BMI	20.63 (19.87-25.2)	23.25 (18.37-23.83)	21.16 (19.81-25)	p=0.809

Mann-Whitney U and chi-squared tests were performed.

OUD: Opioid use disorder, SD: Sexual dysfunction, Bup/Nal: Buprenorphine/Naloxone, PHQ-9: Patient health questionnaire-9, BMI: Body mass index

Table 4. Logistic regression analysis of predictors of sexual dysfunction in women with OUD

	SE	Wald χ^2	P-value	OR	95% CI
Bup/Nal dosage	0.303	4.888	0.027	1.956	[1.079-3.545]
PHQ-9	0.135	6.245	0.012	1.403	[1.076-1.829]

A binary logistic regression analysis was performed

OUD: Opioid use disorder, Bup/Nal: Buprenorphine/Naloxone, PHQ-9: Patient health questionnaire-9, SE: Standard error, P: Statistical significance, OR: Odds ratio, CI: Confidence interval

considerable negative effect on sexual functions (29). Substance use rapidly reduces the response to biological rewards, including sex, and impairs the behaviors that are normally rewarding (30). Additionally, opioid agonists may inhibit the pulsatile secretion of the gonadotropin-releasing hormone in the hypothalamus, leading to hypogonadotropic hypogonadism, which may be one of the other underlying factors between OUD and sexual dysfunctions (31,32). Survivors of cancer who have chronically consumed opioids were shown to have higher levels of sexual dysfunction, which is probably due to similar etiopathogenetic mechanisms (33). However, there are other studies demonstrating better sexual functioning on maintenance compared with treatment-naïve men with OUD (34).

Our results revealed that the dosage of bup/nal treatment is a predictor of sexual dysfunction in women with OUD. Studies on opioid doses (either methadone, buprenorphine/naloxone, or opioids prescribed for pain) have demonstrated contradictory findings regarding their relationship with sexual functions in men (35,36). Zamboni et al. (17) reported a positive correlation between methadone dose and sexual dysfunction in women with OUD; however, this was not present in the but group. Clearly, further evidence accompanied by biological indicators such as gonadotropin and sex hormone levels is needed to determine if a dose-effect relationship exists between SD and opioids.

There are other important factors that can affect the sexual functions of women with OUD. It is noteworthy that traumatic experiences, which affect sexuality, are more common in women with SUDs (27). A higher prevalence of psychiatric comorbidities, such as depression and anxiety, in women with OUD could also contribute to negative sexual functioning (37). In parallel, our results showed that depressive symptoms predict sexual dysfunction in women with OUD, underpinning the need for screening and effective management strategies for psychiatric comorbidities in OUD.

Women with OUD face a plethora of obstacles, such as organizational, financial, social, and psychological issues, which in turn can lead to risks concerning their reproductive health. In our study, we observed that women with OUD used less efficient birth control methods and had higher rates of abortion than the controls. In addition, risky behaviors such as engaging in sexual activity while intoxicated carry the risk of non-consensual sex and sexually transmitted diseases, which are common among women with OUD (38-40). Coupled with OUD, these situations could create greater vulnerability for sexual dysfunction and create barriers to a healthy sexual life.

Study Limitations

The inability to evaluate the baseline sexual functions of patients before OUD diagnosis and the cross-sectional design of the study limit the ability to establish cause-and-effect relationships. Evaluation of sexual functions by self-reporting may have led to recall bias. However, it may have facilitated self-disclosure about sexuality for participants. Although we had a relatively small sample size, it demonstrated substantial differences between the control and OUD groups. Moreover, the limited number of participants may have been a result of the dominance of males with OUD, coupled with women's difficulty in accessing treatment for OUD. Despite its limitations, our article made a valuable contribution to the literature by providing data on sexual dysfunction in women with OUD, which is rarely reported, and comparing it with healthy controls.

Conclusion

These data highlight the unmet sexual and reproductive health needs of women with OUD. Sexual dysfunction is common in women with OUD, which can create a major impediment to adherence to long-term OMT. The presence of depressive symptoms may have a substantial impact on sexual functions; therefore, better screening and intervention strategies should be implemented in routine care for women with OUD. Owing to the common adversities concerning reproductive health, women with OUD could benefit from integrated services in addiction care and sexual and reproductive health.

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Ethics

Ethics Committee Approval: The study was approved by the Clinical Research Ethics Committee of University of Health Sciences Turkey, Erenkoy Training and Research Hospital for Psychiatry and Neurological Diseases (date: 07.04.2023, approval no: 26) and executed in compliance with the regulations set forth in the Declaration of Helsinki and International Conference on Harmonization/Good Clinical Practice guidelines.

Informed Consent: Written informed consent was obtained from all participants before they enrolled in the study.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Concept: E.E.B., R.B., Design: N.G.U.S., M.E., M.K.K., Data Collection or Processing: N.G.U.S., M.E., M.K.K.,

Analysis or Interpretation: N.G.U.S., M.E., Literature Search: N.G.U.S., M.E., Writing: N.G.U.S., M.E., M.K.K., E.E.B., R.B.

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