Psychiatr. Pol. 2022; 56(2): 309–321
PL ISSN 0033-2674 (PRINT), ISSN 2391-5854 (ONLINE)
www.psychiatriapolska.pl
DOI: https://doi.org/10.12740/PP/OnlineFirst/131532

Lower urinary tract symptoms and sexual functioning in patients with depression

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Summary

Aim. A link between sexual functioning and depression has been reported. However, it is still unknown whether lower urinary tract symptoms (LUTS) coexist or correlate with sexual dysfunction (SD) in depressed individuals. Depressed patients represent a unique population because of a possible bidirectional relationship between SD and depression and between LUTS and depression. Thus, the aim of this study was to investigate relationships between depression severity, SD and LUTS for patients with depression.

Material and methods. In this cross-sectional study, we analyzed data on depression, sexual functioning and LUTS from depressed patients who were treated in our department of adult psychiatry. Data were obtained from the *Hamilton Rating Scale for Depression*, the *International Index of Erectile Function* (IIEF), the *Female Sexual Function Index* (FSFI), and the *International Prostate Symptom Score* (IPSS).

Results. We included one hundred two patients diagnosed with, and treated for, depression. The participants reported a high overall prevalence of SD (60.8%), and SD correlated with depression severity. LUTS were also highly prevalent with 86% of the participants reporting at least mild LUTS severity. Despite coexistence of LUTS and SD in multiple patients, we did not find a statistically significant relationship between LUTS and SD in our cohort.

Conclusions. In our exclusive group of individuals diagnosed with, and treated for, depression, depression severity had a negative effect on sexual functioning. Although there was no statistically significant relationship between LUTS and SD, they coexisted in multiple patients. Therefore, LUTS and SD should still be systematically assessed in patients with depression.

Key words: lower urinary tract symptoms, sex, depression

Introduction

Healthy sexual functioning is a significant part of life. Similarly, the ability to experience depression-free moods is vitally important for overall well-being. Therefore, numerous studies have found links between sexual dysfunction (SD) and depression in both men and women [1]. In combination, these disorders may compound the severity of each other; thus, they can have a profoundly negative effect on the quality of life. As many as 70% of depressed individuals may report SD [2]. Although its bidirectional relationship with depression is well documented, SD in depressed patients still remains underestimated, underreported, and undertreated [3].

Recent studies have shown that lower urinary tract symptoms (LUTS) in depressed patients may also be underdiagnosed and often omitted without adequate management [4]. LUTS may lead to isolation, embarrassment, social anxiety, demoralization, loss of self-confidence or motivation, and poor self-esteem, ultimately reducing the quality of life of the patient [5]. Furthermore, there is a growing body of evidence that, like SD and depression, LUTS and depression share a bidirectional relationship wherein each symptom set exacerbates the other [6].

Epidemiological studies have provided consistent evidence for the coexistence of LUTS and SD [7]. In a population of men aged 50-80 years, Seftel et al. found that more than 80% of participants were sexually active with an overall prevalence of LUTS of almost 90% and an overall prevalence of erectile dysfunction (ED) of almost 50% [8]. Salonia et al. reported congruent findings that LUTS and SD often coexisted in women [9].

Depressed patients represent a unique population because of a possible bidirectional relationship between SD and depression and between LUTS and depression. However, it is still unknown whether LUTS and SD coexist or correlate in depressed patients. Most of the studies that assessed connections between LUTS and SD examined only the general population (i.e., mentally healthy persons without a diagnosis of depression or other psychiatric disorders) [7]. Until now, investigators have not examined the complex relationship between depression, SD, and LUTS in patients reliably diagnosed with, and treated for, depression. The relevant information is necessary for a comprehensive understanding of the medical workup and the integrated care that such patients need. Therefore, the aim of this study was to analyze the coexistence and relationships between depression, SD, and LUTS in an exclusive cohort of patients with depression. We hypothesized that depressed patients who reported SD would also often report LUTS.

Materials and methods

This inquiry was a single-center, cross-sectional study, approved by the Bioethics Committee of the Jagiellonian University Medical College in Krakow, Poland (KBET/266/B/2013). All patients provided written informed consent. For the study, we invited adult patients diagnosed with, and treated for, depression, who visited our out-patient and in-patient Department of Adult Psychiatry at the University Hospital

in Krakow between 2014 and 2015. This investigation analyzed questionnaire data on depression severity, SD, and LUTS. All the included patients met both DSM-5 and ICD-10 criteria for depression, and psychiatrists established the diagnoses of all patients. Various demographic data were collected from patient medical records. The following variables were included: age, sex, education, employment status, relationship status, recent hospitalizations due to depression, familial history of depression, and antidepressant medication.

Instruments

Hamilton Rating Scale for Depression

The *Hamilton Rating Scale for Depression* (HRSD), also called the Hamilton Depression Rating Scale, was used to classify depression severity [10]. Its validity to assess symptom load has been proven widely. The HRSD consists of 17 questions with a total score between 0 and 54. For this study, patients were classified as in remission – no depression (0-7), with mild depression (8-16), with moderate depression (17-23), and with severe depression (≥24). Psychiatrists completed the HRSD questionnaire.

International Index of Erectile Function

The *International Index of Erectile Function* (IIEF) is a multidimensional scale for assessment of ED [11]. It is a brief, reliable, self-administered measure of erectile functioning. This scale is cross-culturally valid with the sensitivity and specificity for also detecting treatment-related changes in patients with ED. The IIEF consists of 15 questions with a total score between 5 and 75. The items examine the five main domains of male sexual function, including erectile function (EF), intercourse satisfaction (IS), orgasmic function (OF), sexual desire (SDe), and overall satisfaction (OS). Scores of the different IIEF-15 domains are calculated by summing the scores of the questions representing the domain; the lower the score, the greater the severity of symptoms. The total score consists of scores of all domains. Total scores of 1–5 points on the EF domain indicate that low sexual activity took place in the preceding 4 weeks; in such a case, we could not confirm the diagnosis of ED with the IIEF-15. With the IIEF-15, ED was defined as an erectile function domain score ≤25 points [12]. The severity of ED can be further classified into five categories: no ED (EF score 26 to 30), mild (EF score 22 to 25), mild to moderate (EF score 17 to 21), moderate (EF score 11 to 16), and severe (EF score 6 to 10) [12]. There is no consensus on the cut-off points for normal values in the other domains (i.e., IS, OF, SDe, OS). General intercourse frequency can be estimated with question #6 of the IIEF-15 that covers intercourse frequency. Rynja et al. have proposed that patients be classified as having no intercourse, intercourse <1x/week, and >1x/week [13].

Female Sexual Function Index

The *Female Sexual Function Index* (FSFI) is a widely used measure of female sexual functioning [14]. It is a brief, multidimensional self-report instrument. The FSFI has been shown to discriminate reliably between women with and without SD on each of the six domains: desire, arousal, lubrication, orgasm, satisfaction, and pain [15]. The FSFI consists of 19 questions with a total score between 4 and 95; low scores indicate lower levels of sexual functioning [14]. Scores of the different FSFI domains are calculated by summing the scores of the questions representing the domain. The total score consists of scores of all domains. An analysis of clinical cut-off scores demonstrated that a threshold of ≤26 is reliable for the identification of women with SD [16].

International Prostate Symptom Score

The *International Prostate Symptom Score* (IPSS) was used to assess the severity of LUTS. The IPSS contains seven questions related to urinary storage, voiding, and post micturition symptoms, and one question concerning the quality of life. Because of its simplicity and the versatility and reliability in assessing the severity of LUTS, the IPSS is also used for women. The IPSS scale served as a reference instrument in studies of the association of LUTS and depressive symptoms in the general population [17-19] and the association between LUTS and depression severity of patients clinically diagnosed with depression or neurotic disorders [20, 21]. The total score of the IPSS is between 0 and 35. The final score is assigned to one of the following four severity categories: no symptoms (0), mild (1-7), moderate (8-19), and severe (20-35). The IPSS was designed to be self-administered by the patient.

Statistics

Means, standard deviations, medians, minimum and maximum values (range), and 95% confidence intervals (CI) were used to present descriptive results for continuous data and counts and percent for discrete data. The Shapiro-Wilk test was used to analyze distribution and the Leven (Brown-Forsythe) test was used to investigate the hypothesis of equal variances. To evaluate differences between two groups, we used Student's t-test (or Welch test in the absence of variance homogeneity) or Mann-Whitney U test (if the Student's t-test could not be applied or for variables measured on the ordinal scale). For qualitative variables, we used Chi-square independence test (with Yates' correction for size group less than 10, verification of Cochran conditions, exact Fisher test). Statistical significance was considered when the p value was <0.05. Data analysis was conducted with STATISTICA Software (StatSoft Inc., 2014, ver. 12.0).

Results

Demographics and clinical characteristics

We recruited 106 participants for the study, but 4 patients were eventually excluded because of incomplete questionnaires, thus leaving 102 individuals to be analyzed. The mean age of our cohort was 46.1 (range 20-67) years. There were more women than men. Most of the patients were employed, had higher education, and were in a stable relationship (Table 1).

Table 1. **Demographics of included patients**

Specification	Total, N (%)
Number of included patients	102 (100%)
Sex	
Male	42
Female	60
Education	
Primary	3
Secondary (including students)	45
Higher	54
Employment status	
Employed	55
Unemployed	13
Pensioners	30
Students	4
Relationship status	
Stable relationship/marriage	73
Unstable relationship/marriage	12
Single	17

For our cohort, the mean time between diagnosis of depression and inclusion in the study was 10.7 years. The mean number of hospitalizations related to depression was 2.4 (range 0-20). A familial history of depression was detected in 31 individuals. Our study group was mostly treated with selective serotonin re-uptake inhibitors and serotonin norepinephrine re-uptake inhibitors (Table 2). Some of the participants had concomitant anxiety (n=19), personality (n=4), obsessive-compulsive (n=3), and eating (n=3) disorders. All these patients met specific ICD-10 criteria for their specific concomitant disorders.

Table 2. **Drugs used by the included patients**

Drugs	Number of patients
Antidepressants	
SNRIs	47
SSRIs	46
TCAs	23
NaSSAs	21
SARIs	21
Lithium	14
Other antidepressants	10
Anti-epileptics	
Valproate	23
Lamotrigine	16
Carbamazepine	10
Neuroleptics, first generation	
Phenothiazines	35
Thioxanthenes	13
Butyrophenones	6
Neuroleptics, second generation	
Quetiapine	24
Sulpiride	16
Olanzapine	14
Aripiprazole	8
Other neuroleptics	6
Anxiolytics	
Benzodiazepines	33
Hydroxyzine	10
Buspirone	3

SNRIs – serotonin norepinephrine reuptake inhibitors; SSRIs – selective serotonin reuptake inhibitors; TCAs – tricyclic antidepressants; NaSSAs – noradrenergic and specific serotonergic antidepressants; SARIs – serotonin antagonist and reuptake inhibitors

Of note: Other antidepressants – tianeptine, norepinephrine and dopamine reuptake inhibitors (NDRIs), norepinephrine reuptake inhibitors (NRIs), reversible monoamine oxidase inhibitor (RIMAs), agomelatine. Other neuroleptics – risperidone, clozapine, amisulpride.

Instruments scores

In our study, the mean score of the HRSD questionnaire was 15.9 (range 1-32), and most of our patients experienced mild depression (n=37), followed by moderate depression (n=29), severe depression (n=20), or were in remission (n=16).

The mean score of the IIEF-15 questionnaire was 42.4 (range 5-74). For 6 patients (14% of the men), the EF domain score was ≤5 points. Thirty patients (71% of the men) met the diagnostic threshold of ED with IIEF-15 (i.e., 6 ≤ score ≤ 25 points). Mild ED was noted for 14 patients, mild to moderate ED in 6 patients, moderate ED in 7 patients, and severe ED in 3 patients. In analyzing intercourse frequency during the preceding 4 weeks, we found that 9 patients (21% of the men) did not have an intercourse, 17 patients (41% of male patients) had less than one intercourse per week, and 16 (38% of male patients) had more than one intercourse per week.

The mean score of the FSFI questionnaire was 28.8 (range 4-92). Thirty-two of 60 women (53%) met the diagnostic threshold of SD with FSFI (i.e., score ≤ 26 points).

The mean score from the *International Prostate Symptom Score* (IPSS) was 8.1 (range 0-35). We classified patients as asymptomatic (n=14), mildly symptomatic (n=56), moderately symptomatic (n=24), and severely symptomatic (n=8). Among men with ED (i.e., 6 ≤ IIEF-15 score ≤ 25 points), there were no LUTS-asymptomatic patients, and 17 of 30 (56.7%) men had at least moderate LUTS. Similarly, for women with SD, there were no patients free from LUTS, and 15 (47%) reported at least moderate LUTS.

Relationships

We found significant relationships between depression severity and SD (Table 3). In men, the group of patients with moderate or severe depression had significantly higher risk of ED than the group of patients with remission or mild depression ($p = 0.008$). Furthermore, male patients with moderate or severe depression had lower overall scores from the IIEF-15 than men in remission or with mild depression ($p = 0.0004$). In the female group, patients with moderate or severe depression also had significantly lower overall scores from the FSFI compared with patients in remission or with mild depression ($p = 0.014$). Although depressed men with moderate or severe LUTS tended to have higher risk of ED and lower overall scores from the IIEF-15 than depressed men with mild or no LUTS, these relationships were not statistically significant (Table 4). Similarly, for women, in terms of sexual functioning, we did not find a statistically significant difference between individuals with moderate/severe LUTS and mild/no LUTS.

Table 3. **Characteristic of patients with no depression or mild depression (HRSD score 0-16, Group A) and patients with moderate or severe depression (HRSD score ≥17, Group B) in terms of sexual functioning of men and women**

	Group A	Group B	*P*-value
Men			
IIEF			0.0004[1]

table continued on the next page

Mean (standard deviation)	49.5 (15.4)	33.4 (12.7)	
Range	9.0-64.0	5.0-54.0	
Median	54.5	34.2	
EF			0.0008[1]
Mean (standard deviation)	21.4 (7.5)	16.6 (7.3)	
Range	2.0-32.0	1.0-28.0	
Median	24.5	17.9	
Women			
FSFI			0.014[1]
Mean (standard deviation)	34.8 (32.0)	21.2 (15.3)	
Range	4.0-92.0	2.0-71.0	
Median	15.0	9.5	

[1]Mann-Whitney U test

IIEF – International Index of Erectile Function; EF – Erectile Function domain of IIEF; FSFI – Female Sexual Function Index

Table 4. **Characteristic of patients with no LUTS or mild LUTS (IPSS score 0-7, Group A) and patients with moderate or severe LUTS (IPSS score ≥8, Group B) in terms of sexual functioning of men and women**

	Group A	Group B	*P*-value
Men			
IIEF			0.27461[1]
Mean (standard deviation)	44.6 (18.6)	39.2 (17.1)	
Range	5.0-74.0	7.0-63.0	
Median	49.8	41.5	
EF			0.1909[1]
Mean (standard deviation)	21.5 (10.0)	19.0 (8.2)	
Range	1.0-34.0	1.0-28.0	
Median	25.0	21.5	
Women			
FSFI			0.3851[1]
Mean (standard deviation)	31.9 (29.5)	34.2 (26.4)	
Range	2.0-92.0	5.0-81.0	
Median	17.0	25.0	

[1]Mann-Whitney U test

IIEF – International Index of Erectile Function; EF – Erectile Function domain of IIEF; FSFI – Female Sexual Function Index

Discussion

Clinically significant depression is a leading cause of the global burden of disease, and it is frequently associated with SD in both men and women. It is estimated that individuals with depression have a 50% to 70% increased risk of developing SD, and persons with SD have a 130% to 210% increased risk of developing depression [1]. In our cohort, depression severity and SD correlated well; both men and women with moderate or severe depression had greater impairment of sexual functioning compared with patients in remission or with mild depression. Notably, our study was the first to analyze the coexistence of LUTS and SD in a unique population of patients reliably diagnosed with, and treated for, depression. Although we did not find a statistically significant relationship between LUTS and SD in our cohort, we found that LUTS and SD often coexisted. Therefore, our results, nevertheless, promote the need for multidisciplinary management of depressed patients that includes close cooperation of psychiatrists and urologists. This management approach may also lead to a re-evaluation of current recommendations on diagnosis and treatment of SD in patients with depression [22]. Depressed patients, primarily those reporting SD, should be screened carefully for LUTS. Complex management of this specific patient group should be a priority for different healthcare professionals and a starting point for adequate cooperation.

The current recommendation states that SD should be assessed by a rating scale administered to the patient, instead of relying on spontaneous reporting of symptoms or open questions that may be interpreted differently by different patients [23]. Therefore, a strength of this study is our use of the validated scales for assessment not only of SD but also of depression severity and LUTS. This use of validated scales reduced the possibility of both under – and over-reporting of urological and psychiatric symptoms and sexual functioning. The combined composition of four different reliable questionnaires, including two independent sex-specific instruments for assessment of sexual functioning, ensured reliable results.

Another strength of our study was a homogenous group of depressed patients who all met DSM-5 and ICD-10 criteria for depression. In all cases, psychiatrists confirmed the diagnoses. In addition, all included patients were treated for depression. The study results, therefore, clearly showed the coexistence of SD and LUTS in this specific patient group.

The current literature reports a link between SD and LUTS. Several community-based studies in different geographical regions have provided evidence of an age-independent association between LUTS and ED [24]. As a result, clinicians are encouraged to always evaluate ED in men with LUTS and to take the opportunity to evaluate men who do report ED for LUTS [24]. Similarly, coexistence of SD and LUTS has been reported for women; therefore, investigation of female sexuality is suggested for women reporting LUTS [9]. However, there is still reluctance among all healthcare professionals, including, sometimes, even urologists, to discuss simultaneously sexual functioning and LUTS with patients. Furthermore, if patients are not asked, often they will not volunteer their sexual problems [25]. Because psychiatrists may have limited perception of LUTS in their patients [4], our study highlights the importance of LUTS

assessment in routine clinical practice of physicians who care for depressed patients with concomitant SD. There is still very little evidence for connections between LUTS and SD in depressed patients; therefore, there are still unaddressed, multiple challenges in the complex management of depressed individuals.

We need to consider several pathological pathways shared between depression, SD, and LUTS. First, hypogonadism with low testosterone levels can mimic depressive symptoms, and hypogonadism is associated with poor sexual function [26, 27]. Low-testosterone hypogonadism also contributes to manifestation of LUTS [28]. In women, decreased estrogen levels were shown to be important factors in progression of LUTS, SD, and depressive symptoms [29]. Furthermore, loss of libido is a classic symptom of major depression, and it has a prominent influence in psychodynamic and other psychologic formulations of depressive illness. Systematic studies suggest that low libido is present in up to 75% of depressed patients and results from hormonal imbalance [30]. This overall lack of hormonal homeostasis impairs functioning of both urinary and genital systems. Second, there is a large body of evidence on the untoward effects of antidepressants on sexual functioning [3]. In our study, there was no demonstrable benefit or disadvantage for the use of any specific antidepressant. We can speculate that our analysis was limited by a relatively small sample of drug-free patients and by the absence of a nondepressed comparison sample (placebo group). Cohen et al. made similar observations [31]. The effect of antidepressants on LUTS is still a matter of dispute, and only single studies, mostly case reports, have confirmed positive associations between LUTS and antidepressants [32]. Finally, a hypothesis that LUTS, SD, and depression share a common neurochemical pathogenesis can partially explain the presented relationship. Altered concentrations of serotonin and norepinephrine in the central nervous system and increased adrenergic tone with impairment of the hypothalamic-pituitary axis may also affect the associations between LUTS, SD, and depression severity/depressive symptoms [6].

Our study is not free from limitations. We acknowledge that the evaluated patients represented a highly selected cohort, treated at a single, high-volume academic center; thus, the results may not be fully transferable to routine clinical practice for all patients treated for depression. In the analysis, we focused on the total scores from the questionnaires, which represent general SD. We also attempted to perform statistical analyses on each of the questionnaire clusters that may have further differentiated various types of SD. However, we were not able to identify consistent relationships between specific types of SD. Although our sample size was large enough for powerful statistical analysis, possibly, the study lacked adequate power for specific and detailed analyses. Similarly, it is possible that we would have found statistically significant connections between LUTS and SD with a larger sample size.

Conclusions

This exclusive study has shown a coexistence of LUTS, SD, and depression. SD and LUTS were present in a substantial percentage of our cohort of patients who were treated for clinically validated depression. Even without statistically significant

relationships between LUTS and SD, healthcare professionals who care for depressed patients should still screen for both SD and LUTS because of the coexistence of these two conditions. Our study can be a basis for improvement in patient-centered care of depressed individuals.

Declarations
Funding: this study was not sponsored.
Conflicts of interest: the authors declare that they have no conflict of interests.

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