Impairment of Sexual Desire in Treatment-Resistant Depression: Prevalence and Correlates

Walter dos Santos Gonçalves, MD, MSc[a,b,*]; Roseane Dorte Halkjaer Lassen, BSN[a]; Aline Sardinha, PhD[b]; Evandro Silva Freire Coutinho, MD, PhD[c]; David S. Baldwin, MD, DM[d,e]; Antonio E. Nardi, MD, PhD[a]; and Jose Carlos Appolinario, MD, PhD[a]

ABSTRACT

Objective: To assess sexual desire in patients with treatment-resistant depression (TRD).

Methods: Baseline data were analyzed from an ongoing cohort study at an outpatient clinic specializing in TRD treatment in Brazil. The cohort comprised consecutive patients with the diagnosis of TRD who sought treatment at this center between November 2015 and January 2021. The Hamilton Depression Rating Scale (HDRS) genital symptoms item (item 14) was used as a proxy to assess sexual desire.

Results: Sixty-five participants with TRD were included. There was sexual desire impairment in 67.7% of patients. Men (87.5%) were more affected than women (61.2%), and this difference was statistically significant ($P = .05$). Depression severity was associated with greater complaints of this aspect of sexual function ($P < .01$).

Conclusions: Participants with TRD had a high prevalence of sexual desire impairment, which was associated with greater depressive symptom severity and male sex. The findings suggest that health care professionals should systematically assess sexual desire in patients with TRD in daily clinical practice. Further longitudinal studies are needed in larger samples using specific instruments for assessing sexual dysfunction and comparing TRD and non-TRD populations.

Prim Care Companion CNS Disord 2022;24(6):22m03275

To cite: Gonçalves WS, Lassen RDH, Sardinha A, et al. Impairment of sexual desire in treatment-resistant depression: prevalence and correlates. *Prim Care Companion CNS Disord.* 2022;24(6):22m03275.

To share: https://doi.org/10.4088/PCC.22m03275

[a]Treatment-Resistant Depression Outpatient Clinic, Institute of Psychiatry, Federal University of Rio de Janeiro, Rio de Janeiro, Brazil

[b]Sexual Dysfunction Unit, Institute of Psychiatry, Federal University of Rio de Janeiro, Rio de Janeiro, Brazil

[c]Department of Epidemiology, Institute of Social Medicine, State University of Rio de Janeiro, Rio de Janeiro, Brazil

[d]Clinical and Experimental Sciences, Faculty of Medicine, University of Southampton, Southampton, United Kingdom

[e]Department of Psychiatry and Mental Health, University of Cape Town, Cape Town, South Africa

**Corresponding author:* Walter dos Santos Gonçalves, MD, MSc, Outpatient Clinic—Institute of Psychiatry-UFRJ, Av. Venceslau Bras, 71 Fundos, 22290-160, Botafogo, Rio de Janeiro, Brazil (wsg1989@gmail.com).

Depression is a high prevalence psychiatric disorder, and sexual dysfunction is a common complaint in individuals with this condition.[1–3] A recent meta-analysis[2] found that the most frequent sexual dysfunction in major depressive disorder (MDD) was decreased sexual desire, affecting 65.3% of women and 40.3% of men. Although there are increasing data about sexual dysfunction in MDD, little is known about sexual functioning in patients with treatment-resistant depression (TRD).

Several hypotheses have been proposed to explain this relationship, such as the presence of anhedonia, which is a common symptom of depression. Evidence suggests that simultaneous changes in affective symptoms and sexual function may result from shared underlying mechanisms. Thus, depressive mood and anhedonia are both implicated in the capability to express sexual desire.[4,5] Another assumption is that treatment-emergent sexual adverse effects, common with several antidepressants, are responsible for reducing dopamine activity in the mesolimbic system through 5-HT_2 receptors, often resulting in decreased sexual desire.[6]

Some define TRD as a failure to respond to at least 2 adequate pharmacologic treatment regimens. However, there is no clear consensus on this condition, as we cannot infer that there are substantial differences between patients without symptom remission after 1 or 2 antidepressant courses.[7] As TRD tends to be a chronic, recurrent, more severe condition requiring multiple pharmacologic strategies,[8] sexual desire is expected to be more impaired in this population. Thus, the objective of this study was to estimate the prevalence and correlations of sexual desire impairment in outpatients attending a clinic specializing in TRD treatment in Brazil.

METHODS

This was a cross-sectional analysis of baseline data from an ongoing cohort study of patients with TRD. This cohort comprises consecutive patients seeking treatment from the Treatment-Resistant Depression Research Group (DeReTrat) at the Institute of Psychiatry, Federal University of Rio de Janeiro. The study was approved by the local independent ethics committee (registration number: 13978719.0.0000.5263), and all individuals provided written informed consent before participation.

Study Population

Individuals were aged ≥ 18 years and fulfilled diagnostic criteria for MDD according to the *DSM-IV*. In this study, TRD was

Clinical Points

- The overall prevalence of sexual desire impairment in patients with treatment-resistant depression (TRD) was 67.7%.
- The presence of sexual desire symptoms in TRD was associated with higher depression severity and male sex.
- Sexual dysfunction is highly prevalent in patients with depressive disorders; future research comparing sexual dysfunction in TRD and non-TRD populations should be conducted to address the differences between these conditions.

characterized by the failure to respond to at least 1 adequate pharmacologic trial. MDD was the main diagnosis, and participants with psychotic disorders, intellectual impairment, bipolar disorder, dementia, or substance use disorders as a primary disorder were excluded. Pregnant or lactating women were also excluded.

Assessment Scales

The Mini International Neuropsychiatric Interview Brazilian version 5.0.0 for *DSM-IV*[9] was used to assess MDD diagnostic criteria. The Massachusetts General Hospital Antidepressant Treatment Response Questionnaire[10] was used to assess treatment resistance. The Hamilton Depression Rating Scale 21-item version (HDRS-21)[11] was used to evaluate depression severity and sexual desire impairment. In previous research, item 14 (genital symptoms) of the HDRS-21 has been used as a proxy to assess sexual desire impairment.[11,12] This item evaluates both sexual desire and menstrual disturbances and is scored between 0 and 2.

Data Collection

Participants were evaluated by medical residents in psychiatry trained in the diagnosis and treatment of TRD. All researchers were trained in the application of the instruments used in this study. Two researchers (W.S.G. and R.D.H.L.) collected baseline data from patients seeking treatment between November 2015 and January 2021.

Demographic data (including age, sex, race, marital status, and schooling) were collected, as well as data about MDD characteristics (number of previous episodes, current episode duration, age at onset of the first episode) and medication used. Depression severity data were assessed by total HDRS score.

Statistical Analysis

Means and proportions were calculated for sociodemographic and clinical variables, stratified by the presence or absence of sexual symptoms. Statistical significance for the difference between the 2 groups was evaluated using Kruskal-Wallis test (means) and χ^2 statistic (proportions). *P* values ≤ .05 were considered statistically significant. All analyses were performed using Stata 16.1 software.

RESULTS

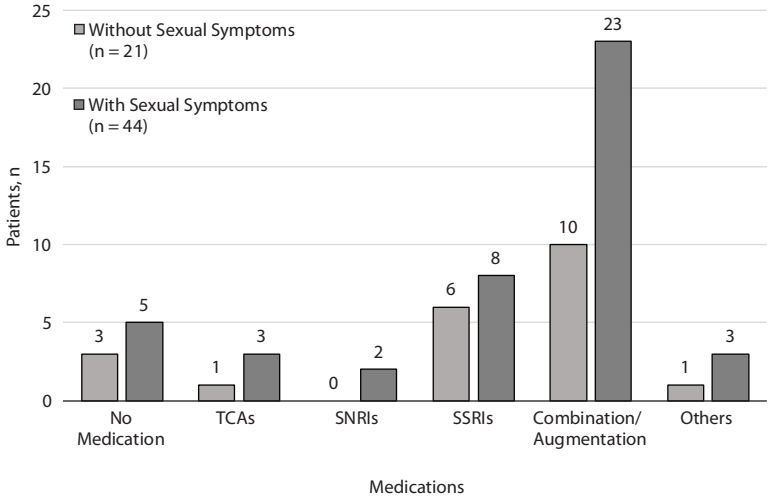
Sixty-five participants were included in the study. The mean (SD) age was 52.46 (12.75) years, and 75% were female. Most participants were highly educated, not married, and had moderate to severe depression (mean [SD] HDRS score: 22.18 [6.02]), and approximately half were using combination/augmentation treatment strategies (n = 33). Forty

Table 1. Sociodemographic and Clinical Characteristics of the Sample[a]

Characteristic	Without Sexual Symptoms (n = 21)	With Sexual Symptoms (n = 44)	*P* Value
Age, mean (SD), y	52.04 (15.80)	52.67 (11.17)	.89
Race			.65
White	36.1 (13)	63.9 (23)	
Non-White	30.4 (7)	69.6 (16)	
Sex			.05
Male	12.5 (2)	87.5 (14)	
Female	38.8 (19)	61.2 (30)	
Marital status			.55
Married	28 (7)	72 (18)	
Single/divorced/widowed	35 (14)	65 (26)	
Education, y			.65
0–8	20 (2)	80 (8)	
9–12	33.3 (7)	66.7 (14)	
> 12	35.5 (11)	64.5 (20)	
No. of episodes			.36
Single episode	37.1 (13)	62.9 (22)	
Recurrent episodes	26.7 (8)	73.3 (22)	
Episode duration, y			.53
≤ 1	37.5 (9)	62.5 (15)	
> 1	30 (12)	70 (28)	
MDD severity (HDRS score)			< .01
Total score, mean (SD)	19.47 (5.44)	23.47 (5.91)	
No. of medications, mean (SD)	2.14 (1.5)	2.31 (1.4)	.56
Treatment resistant			.61
Resistant to 1 antidepressant	36 (9)	64 (16)	
Resistant to ≥ 2 antidepressants	30 (12)	70 (28)	

[a]Values are presented as n (%) unless otherwise specified.
Abbreviations: HDRS = Hamilton Depression Rating Scale, MDD = major depressive disorder.

Figure 1. Medications of the Sample[a]



[a]Augmentation: association between antidepressant and other agents except benzodiazepines or Z-drugs. Combination: ≥ 2 antidepressants combined. Others: clonazepam, lamotrigine, bupropion, agomelatine.
Abbreviations: SNRIs = serotonin-norepinephrine reuptake inhibitors, SSRIs = selective serotonin reuptake inhibitors, TCA = tricyclic antidepressants.

(61.5%) patients had not responded to at least 2 adequate pharmacologic treatment regimens, and 25 (38.5%) had not responded to a single course of an antidepressant.

We found a prevalence of sexual desire impairment of 67.7% (n = 44). Of those, 11 (25%) subjects had a mild and 33 (75%) a more severe impairment. The prevalence in men was 87.5% and in women was 61.2%, and this difference was statistically significant ($P = .05$). The presence of sexual symptoms was associated with higher MDD severity ($P < .01$). The difference between other variables was not statistically significant when both groups (with or without impairment in sexual desire) were compared. The main findings are summarized in Table 1 and Figure 1.

DISCUSSION

This is the first study, to our knowledge, assessing sexual desire impairment in TRD. The overall prevalence of sexual desire impairment (67.7%) accords with findings from a systematic review[2] that evaluated sexual dysfunction in MDD (38.3%–76.0%). Although the prevalence of desire impairment in women in our study is similar to the findings of that review,[2] the prevalence of impairment in men in our study was somewhat higher. In a meta-analysis[6] of treatment-emergent sexual dysfunction associated with antidepressants, the prevalence of sexual desire dysfunction was higher in men compared to women. Our finding of a significant association between depressive symptom severity and presence of sexual impairment aligns with previous findings.[13–15]

Our study has 2 major limitations. The absence of a specific sexual assessment instrument may have impacted the findings, given that the HDRS genital item was not made for this specific purpose, as it also assesses menstrual disturbances in women. Furthermore, the relatively small sample size reduces the statistical power to detect the difference between groups and may affect the generalizability of the study findings. However, strengths of the study are that it is the first investigation of sexual desire impairment in patients with TRD, assessments were conducted with validated scales by trained psychiatrists, and the inclusion of consecutive patients reduces selection bias.

The link between sexual dysfunction and failure to achieve symptom remission in patients with MDD,[16] and the association between treatment-emergent sexual dysfunction and lower medication adherence (thereby increasing the risk of relapse and recurrence of depressive episodes),[17,18] suggests at least some common underlying mechanisms. Serretti and Chiesa[6] found that several selective serotonin reuptake inhibitors (SSRIs) and serotonin-norepinephrine reuptake inhibitors (SNRIs) were associated with sexual desire impairment,[6] and the incidence of treatment-emergent sexual dysfunction with SSRIs or SNRIs has been estimated to be around 40%–50%.[5,19] In our sample, most participants were prescribed these antidepressant classes. Another possible explanation for this finding is the sample age, as sexual difficulties are associated with increasing age.[20] Future longitudinal studies with large samples should use specific validated sexual assessment instruments to compare sexual functioning in TRD and non-TRD populations.

CONCLUSION

Participants with TRD had a high prevalence of sexual desire impairment, which was associated with male sex and higher depressive symptom severity. Future investigations should employ larger samples and use specific sexual assessment instruments, comparing patients with or without TRD.

Submitted: March 2, 2022; accepted May 13, 2022.
Published online: November 22, 2022.
Relevant financial relationships: None.
Funding/support: None.

REFERENCES

1. Gonçalves WS, Gherman BR, Abdo CHN, et al. Função e disfunção sexual na depressão: uma revisão sistemática. *J Bras Psiquiatr*. 2019;68(2):110–120.
2. Gonçalves WS, Gherman BR, Abdo CHN, et al. Prevalence of sexual dysfunction in depressive and persistent depressive disorders: a systematic review and meta-analysis [published online ahead of print February 21, 2022]. *Int J Impot Res*. 2022.
3. Baldwin DS, Foong T. Antidepressant drugs and sexual dysfunction. *Br J Psychiatry*. 2013;202(6):396–397.
4. Kalmbach DA, Ciesla JA, Janata JW, et al. Specificity of anhedonic depression and anxious arousal with sexual problems among sexually healthy young adults. *J Sex Med*. 2012;9(2):505–513.
5. Montejo AL, Montejo L, Baldwin DS. The impact of severe mental disorders and psychotropic medications on sexual health and its implications for clinical management. *World Psychiatry*. 2018;17(1):3–11.
6. Serretti A, Chiesa A. Treatment-emergent sexual dysfunction related to antidepressants: a meta-analysis. *J Clin Psychopharmacol*. 2009;29(3):259–266.
7. Gaynes BN, Lux L, Gartlehner G, et al. Defining treatment-resistant depression. *Depress Anxiety*. 2020;37(2):134–145.
8. Kautzky A, Dold M, Bartova L, et al. Clinical factors predicting treatment resistant depression: affirmative results from the European multicenter study. *Acta Psychiatr Scand*. 2019;139(1):78–88.
9. Amorim P. Mini International Neuropsychiatric Interview (MINI): validação de entrevista breve para diagnóstico de transtornos mentais. (Mini International Neuropsychiatric Interview [MINI]: validation of a short structured diagnostic psychiatric interview). *Rev Bras Psiquiatr*. 2000;22(3):106–115.
10. Chandler GM, Iosifescu DV, Pollack MH, et al. RESEARCH: validation of the Massachusetts General Hospital Antidepressant Treatment History Questionnaire (ATRQ). *CNS Neurosci Ther*. 2010;16(5):322–325.
11. Kennedy S. Flibanserin: initial evidence of efficacy on sexual dysfunction, in patients with major depressive disorder. *J Sex Med*. 2010;7(10):3449–3459.
12. Freeman MP, Fava M, Dirks B, et al. Improvement of sexual functioning during treatment of MDD with adjunctive pimavanserin: A secondary analysis. *Depress Anxiety*. 2020;37(5):485–495.
13. Fabre LF, Smith LC. The effect of major depression on sexual function in women. *J Sex Med*. 2012;9(1):231–239.
14. Fabre LF, Clayton AH, Smith LC, et al. Association of major depression with sexual dysfunction in men. *J Neuropsychiatry Clin Neurosci*. 2013;25(4):308–318.
15. Bonierbale M, Lançon C, Tignol J. The ELIXIR study: evaluation of sexual dysfunction in 4,557 depressed patients in France. *Curr Med Res Opin*. 2003;19(2):114–124.
16. Saragoussi D, Touya M, Haro JM, et al. Factors associated with failure to achieve remission and with relapse after remission in patients with major depressive disorder in the PERFORM study. *Neuropsychiatr Dis Treat*. 2017;13:2151–2165.
17. Burra TA, Chen E, McIntyre RS, et al. Predictors of self-reported antidepressant adherence. *Behav Med*. 2007;32(4):127–134.
18. Clayton AH, El Haddad S, Iluonakhamhe JP, et al. Sexual dysfunction associated with major depressive disorder and antidepressant treatment. *Expert Opin Drug Saf*. 2014;13(10):1361–1374.
19. Williams VSL, Edin HM, Hogue SL, et al. Prevalence and impact of antidepressant-associated sexual dysfunction in three European countries: replication in a cross-sectional patient survey. *J Psychopharmacol*. 2010;24(4):489–496.
20. Laumann EO, Paik A, Rosen RC. Sexual dysfunction in the United States: prevalence and predictors. *JAMA*. 1999;281(6):537–544.