

## SEXUAL DYSFUNCTION IN PATIENTS WITH EPILEPSY

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### SUMMARY

**Background:** Patients with epilepsy commonly report sexual dysfunction (SD) and reproductive difficulties. This study aimed to evaluate the relationship between epilepsy, antiepileptic drugs (AEDs) and SD, and its association with the quality of life and depressive symptoms.

**Subjects and methods:** This was a prospective study carried out in a tertiary healthcare centre. SD was evaluated using the internationally acclaimed questionnaire Arizona Sexual Experiences Scale (ASEX) that was successfully translated into Croatian and validated for this purpose. Depressive symptoms and quality of life were evaluated using the Hamilton Rating Scale for Depression (HAM-D17) and Quality of life in epilepsy-31 inventory (QOLIE-31).

**Results:** Of 108 patients (68 (63 %) women, 40 (37 %) men, mean age 39.54±15.91 (range 18-80) years) with epilepsy, 16 (14.8%) had focal, 38 (35.2%) generalized and 44 (40.7%) both types of epilepsy. Mean overall total score on the ASEX questionnaire was 11.94±5.61 (mean total score women 12.85±6.00, mean total score men 10.4±4.55), with 48 reporting that they had sexual activity in the past week. Nine (8.33%) patients (7 (6.48%) women, 2 (1.85%) men, mean age 47.66±19.33 (range 25-80) years) had a score 19 and above, 38 (35.18%) patients (27 (25%) women, 9 (8.33%) men, mean age 46.82±17.78 (range 19-80) years) individual score 5 and above on any one item, and 33 (30.55%) patients (26 (24.07%) women, 7 (6.48%) men, mean age 48.87±17.8 (range 19-80) years) had an individual score 4 and above on any three items. Significant correlations were found between SD and older age ( $p=0.001$ ) and between more pronounced symptoms regarding SD on ASEX and female gender ( $p=0.000$ ). There were no significant correlations between the type of epilepsy and SD, nor between the AEDs (old generation vs. modern) and SD. Significant correlations were found between the SD and more pronounced depressive symptoms ( $p=0.003$ ) and between the SD and a lower quality of life ( $p=0.001$ ).

**Conclusions:** Results of our study suggest SD is experienced by around one-third of patients in our group, which is similar to the previous percentage of SD reported in the community sample. Women were found to experience more pronounced symptoms of SD on ASEX. Symptoms of SD were found to be significantly correlated with older age, female gender, lower quality of life and depressive symptoms, while no significant correlations were found with the type of epilepsy and the AEDs.

**Key words:** epilepsy - sexual dysfunction (SD) - Arizona Sexual Experiences Scale (ASEX) – depression - quality of life (QoL)

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### INTRODUCTION

According to International League Against Epilepsy (ILAE) practical definit of epilepsy from 2014, epilepsy is a disease of the brain defined by any of the following conditions: (1) At least two unprovoked (or reflex) seizures occurring >24 h apart; (2) one unprovoked (or reflex) seizure and a probability of further seizures similar to the general recurrence risk (at least 60%) after two unprovoked seizures, occurring over the next 10 years; (3) diagnosis of an epilepsy syndrome (Fisher 2014).

Around 50 million people worldwide are estimated to have epilepsy, making it one of the most common neurological diseases globally.

The World Health Organisation (WHO) defines sexual health as a state of physical, emotional, mental and social well-being in relation to sexuality (WHO 2019).

Reported rates of sexual dysfunction (SD) in epilepsy patients vary. Recently published meta-analysis reports rates of SD in patients with epilepsy and controls 58.1% vs. 16.5%, in men 58.6% vs. 9.8%, and women 59.1% vs. 19.5% (Kronemyer 2019, Zhao 2019).

Different predisposing factors have been proposed as possible contributing factors, e.g. dysregulation of the hypothalamic-pituitary-gonadal axis, comorbid neuropsychiatric disorders (i.e. depression and anxiety), and even antiepileptic drugs (AEDs) (Yang 2016, Zhao 2019).

However, little is known about the prevalence of SD in patients with epilepsy in Croatia, and this study aimed to evaluate the relationship between epilepsy, antiepileptic drugs (AEDs) and SD, and its association to the quality of life (QoL) and depressive symptoms in our group of patients.

## SUBJECTS AND METHODS

This was a prospective cross-sectional study that was carried out at the tertiary teaching hospital (University Hospital Center Zagreb, Croatia) with ethics committee approval.

Three questionnaires evaluating SD, depressive symptoms and QoL were administered to consecutive patients in outpatient's clinic for epilepsy patients (Referral Centre of the Ministry of Health of the Republic of Croatia for Epilepsy, Zagreb, Croatia).

SD was evaluated using the internationally acclaimed and valid questionnaire Arizona Sexual Experience Scale (ASEX). This questionnaire enquires about the overall level of SD during the previous week, including the day of completing the questionnaire. There are 5 questions, each

response is scored from '1 - extremely strong' to '6-no sex drive', with the total score from 5 to 30, and a higher score signifying more pronounced symptoms of SD. SD is defined, as suggested by the authors of this questionnaire, as a total 19 or more, or 5 or more on any item, or 4 or more on three items (Arizona Board of Regents, University of Arizona 1997, McGahuey et al. 2000, Simple and Practical Mental Health 2021). With permission we translated this questionnaire into Croatian, and also conducted validation tests: internal consistency/ reliability was found to be good to excellent (range 0.878-0.929), stability (test-retest reliability) was found to be very high for the majority of questions (>0.9), and content/face validity was also found to be good (Table 1, 2, 3).

Depressive symptoms were evaluated using the Hamilton Rating Scale for Depression (HAM-D17) (Hamilton 1960) and QoL was assessed using Quality of life in epilepsy-31 inventory (QOLIE-31) (Cramer et al. 1998, 2003, Lusic et al. 2011). The results of the latter two questionnaires are not the focus of this paper and their purpose here was to give an insight into the relationship between the SD and depressive symptoms and SD and QoL in epilepsy patients.

**Table 1.** Cronbach's alpha Internal consistency overall on ASEX was found to be good to excellent

	Scale Mean if Item Deleted	Scale Variance if Item Deleted	Item-Total Statistics		Cronbach's Alpha if Item Deleted
			Corrected Item-Total Correlation	Squared Multiple Correlation	
ASEX 1	6.60	7.273	0.879	0.782	0.907
ASEX 2	6.86	7.381	0.891	0.798	0.899
ASEX 3 Male/Female	6.99	6.853	0.855	0.732	0.929

ASEX - Arizona Sexual Experiences Scale

**Table 2.** Cronbach's alpha Internal consistency on ASEX for the group that had sexual activity in the past week was found to be good to excellent

	Scale Mean if Item Deleted	Scale Variance if Item Deleted	Item-Total Statistics		Cronbach's Alpha if Item Deleted
			Corrected Item-Total Correlation	Squared Multiple Correlation	
ASEX 1	11.20	16.294	0.731	0.765	0.895
ASEX 2	11.33	15.958	0.818	0.794	0.879
ASEX 3 Male/Female	11.50	15.411	0.813	0.697	0.878
ASEX 5	11.37	15.438	0.708	0.667	0.902
ASEX 6	11.74	14.686	0.791	0.726	0.883

ASEX - Arizona Sexual Experiences Scale

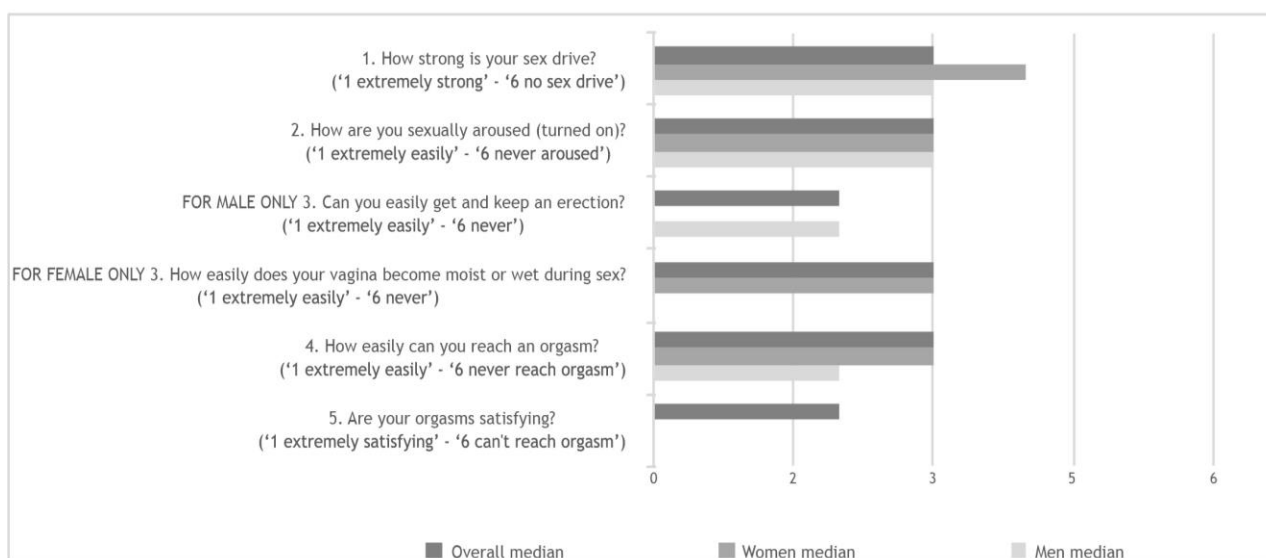
**Table 3.** Stability (test-retest reliability) was found to be very high for majority of questions (>0.9)

	Valid	Missing
1. How strong is your sex drive? (1 - extremely strong; 6 - no sex drive)	101	7
2. How are you sexually aroused (turned on)? (1 - extremely easily; 6 - never aroused)	99	9
<i>Male only</i>		
3. Can you easily get and keep an erection? (1 - extremely easily; 6 - never)	38	70
<i>Female only</i>		
3. How easily does your vagina become moist or wet during sex? (1 - extremely easily; 6 - never)	59	49
4. How easily can you reach an orgasm?(1 - extremely easily; 6 - never reach orgasm)	48	60
5. Are your orgasms satisfying? (1 - extremely satisfying; 6 - can't reach orgasm)	48	60

**Table 4.** Key features of our group of patients with epilepsy

Patients with epilepsy	<i>N</i> =108 - mean age 39.54±15.91 (range 18-80) years <i>Women</i> 63% ( <i>n</i> =68) - mean age 38.07±16.14 (18-77) years <i>Men</i> 37% ( <i>n</i> =40) - mean age 42.102±15.37 (18-80) years
Type of epilepsy	<i>Focal</i> - <i>n</i> =16 (14.8%) <i>Generalised</i> - <i>n</i> =38 (35.2%) <i>Both types of epilepsy</i> - <i>n</i> =44 (40.7%)
AEDs	<i>Newer AED</i> - <i>n</i> =37 (34.2%) <i>Both older and newer AED</i> - <i>n</i> =34 (31.4%) <i>Older AED</i> - <i>n</i> =17 (15.7%) <i>Monotherapy</i> - <i>n</i> =27 (25%): <i>Two and more AED</i> - <i>n</i> =71 (65.74%)
ASEX	<i>Mean total score on the ASEX questionnaire</i> Overall 11.94±5.61 Women 12.85±6.00 Men 10.4±4.55 <i>Total score 19 and above on ASEX</i> Overall <i>n</i> =9 (8.33%) Women <i>n</i> =7 (6.48%) Men <i>n</i> =2 (1.85%) <i>Mean individual score 5 and above on any one item on ASEX</i> Overall <i>n</i> =38 (35.18%) Women <i>n</i> =27 (25%) Men <i>n</i> =9 (8.33%) <i>Individual score 4 and above on any three items on ASEX</i> Overall <i>n</i> =33 (30.55%) Women <i>n</i> =26 (24.07%) Men <i>n</i> =7 (6.48%)

AEDs - antiepileptic drugs; ASEX - Arizona Sexual Experiences Scale



ASEX - Arizona Sexual Experiences Scale

**Figure 1.** Median responses on each question on ASEX overall, in women and in men

Statistical analysis was performed using statistical software IBM Corp. released in 2011. IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp, using t-test, one way ANOVA, post hoc Scheffe test, Bonferroni, Tukey test and Pearson correlation coefficient.

## RESULTS

108 patients (63% (*N*=68) women, 37% (*N*=40) men; mean age overall 39.54±15.91 (range 18-80) years, women 38.07±16.14 (18-77) years, men 42.102±15.37 (18-80) years). 16 (14.8%) patients had focal, 38 (35.2%)

generalised and 44 (40.7%) patients both types of epilepsy. Majority of patients (24%) were in the age group between 26 to 35 years. Majority of patients (N=71 (65.74%)) were on two and more AED, while one-quarter was treated with monotherapy (N=27 (25%). Mean overall total score on the ASEX questionnaire was  $11.94 \pm 5.61$  (mean total score women  $12.85 \pm 6.00$ , mean total score men  $10.4 \pm 4.55$ ), with 48 reporting that they had sexual activity in the past week (Table 4).

When looking specifically into each response per question on the ASEX questionnaire (Figure 1), the overall median was 3, in women 3, and in men 2, with women (unlike men) mainly reporting that they had sexual activity in the past week (women n=33 vs. men n=15). When looking at median responses on ASEX, the highest score in women was found concerning sex drive (median 4), and in men regarding sex drive and arousal (both median 3).

The overall mean response for men on ASEX was  $2.72 \pm 0.29$  (2.4-3.12), and for women  $3.43 \pm 0.47$  (2.69-3.93).

Total score 19 and above was found in 8.33% (N=9, 6.48% (N=7) women, 1.85% (N=2) men, mean age in this group of patients  $47.66 \pm 19.33$  (range 25-80) years, women mean age  $45.71 \pm 16.17$  (range 25-68) years, men mean age  $54.5 \pm 36.06$  (range 29-80) years)) of patients with the overall responses measured mean on the ASEX questionnaire  $4.44 \pm 0.89$  (vs.  $3.12 \pm 1.34$  in the group with the lower score).

Mean individual score 5 and above on any one item was found in 35.18% (N=38, 25% (N=27) women, 8.33% (N=9) men, mean age in this group of patients was  $46.82 \pm 17.78$  (range 19-80) years, women mean age  $44.18 \pm 17.82$  (range 19-72) years, men mean age  $55.75 \pm 15.44$  (range 29-80) years) of patients with the overall responses measured mean on the ASEX questionnaire  $4.76 \pm 1.21$  (vs.  $2.57 \pm 0.72$  in a group with the lower score).

Individual score 4 and above on any three items were found in 30.55% (N=33, 24.07% (N=26) women, 6.48% (N=7) men, mean age in this group of patients was  $48.87 \pm 17.8$  (range 19-80) years, women mean age  $46.11 \pm 17.62$  (range 19-72) years, men mean age  $59.14 \pm 15.51$  (range 29-80) years) of patients with the overall responses measured mean on the ASEX questionnaire  $4.76 \pm 1.08$  (vs.  $2.57 \pm 0.81$  in a group with the lower score).

Regarding the question about genital symptoms on HAM-D17, majority of patients (N=67, 62.03%, 42 women, 25 men) did not have any symptoms, mild symptoms were found in 18.51% (N=20, 12 women, 8 men), while severe symptoms were found in 8.3% (N=9, 7 women, and 2 men).

Significant correlations were found between more pronounced SD symptoms and older age ( $p=0.001$ ). More pronounced symptoms of SD on ASEX were also

found significantly more often in women ( $p=0.000$ ). More pronounced symptoms of SD were found to be in significant correlation with depressive symptoms ( $p=0.003$ ), as well as with the lower QoL ( $p=0.001$ ).

Type of epilepsy and the AEDs (old generation vs. modern) were not found to significantly correlate with more pronounced SD symptoms.

## DISCUSSION

There are wide variations in the reported prevalence of SD, with nearly one-half of men and women with epilepsy reported to have SD, but in the majority, this often goes unnoticed (Rathore et al. 2019).

Little is known about the prevalence of SD in patients with epilepsy in Croatia, and this study aimed to assess whether our patients with epilepsy also experience SD symptoms and to see which of those SD symptoms are most prominent. For this purpose, the ASEX questionnaire, the questionnaire commonly used in clinical trials to assess sexual functioning, was, with permission translated, and successfully validated for Croatian language (McGahuey et al. 2000, Simple and Practical Mental Health 2021).

Very often addressing this topic requires a multi-disciplinary approach, and we find that this scale is a very practical tool that helps a clinician quickly screen for SD symptoms, and in the long run helps with optimization of the management (Atif et al. 2016).

Results of our study suggest that SD, as defined by the authors of this scale, is experienced by around one-third of our patients.

These results are somewhat lower than the results of a recent meta-analysis that on studies using different assessment tools (ASEX, Female Sexual Function Index (FSFI)), International Index of Erectile Function (IIEF), defined sexual functioning questionnaire, 4th Edition (DSM IV) and 5th Edition (DSMV)) found SD to be present in 58.1% of patients with epilepsy vs. 16.5% controls (Zhao 2019).

Interestingly enough, the mean age of our group of patients that satisfied criteria for SD according to ASEX was around 47 years, demonstrating how this issue can have an impact on a younger population. As expected (Camacho & Reyes-Ortiz 2005), our study also found older age to be associated with more pronounced symptoms of SD.

Although SD was previously found to be associated with focal epilepsy and enzyme-inducing and multiple AEDs (Rathore et al. 2019, Yogarajah & Mula. 2017), our study did not find the relationship between the type of epilepsy, nor between the AEDs (old generation vs. modern) and SD.

This could be explained by the significant heterogeneity among the studies concerning the patient population, type and severity of epilepsy, number and type of

AEDs used, and different tools used for assessing sexual dysfunction (Rathore et al. 2019).

In accordance with previous studies, the results of our study also demonstrate the correlation between the SD with the lower QoL and depressive symptoms (Rathore et al. 2019).

More women were found to have SD according to ASEX. This is particularly important since women throughout their lifespan encounter specific challenges potentially affecting not only sexual but also reproductive health (Bangar et al. 2016).

Women had in general higher responses on ASEX on all questions, signifying more pronounced symptoms of SD. Women with epilepsy generally report dysfunction in the domains of desire, which corresponds with our findings, with women in our study reporting most issues with sex drive. This was also true for men in our study, men reporting most issues with sex drive and arousal, who in general report arousal disorders such as erectile dysfunction and premature ejaculation (Rathore et al. 2019).

The overall median on ASEX questionnaire was 3, signifying 'somewhat strong' / 'somewhat easily' / 'somewhat satisfying', which would indicate that overall SD symptoms were not found to be that pronounced in our group of patients.

The limitation of this study was that there was no control group. When looking into previous studies on this matter, the similar percentages of SD as found by our study were earlier reported in both women and men in a healthy population in Croatia (Stulhofer et al. 2005, Stulhofer & Bajic 2006).

Since our study did not find a correlation between the SD and the type of epilepsy, nor AEDs, we may say that findings in our group of patients with epilepsy are similar to the prevalence of SD noted in community samples. A larger properly designed study is needed to evaluate further this issue.

## CONCLUSIONS

Care of patients with epilepsy should include enquiring about SD and a questionnaire may be a helpful tool in addressing this issue. This study evaluated the presence of SD in patients with epilepsy in Croatia and for this purpose, the internationally acclaimed questionnaire ASEX was successfully translated into Croatian and validated. Results of our study suggest SD is experienced by around one-third of patients in our group, which is similar to the previous percentage of SD reported in the community sample. Women were found to experience more pronounced symptoms of SD on ASEX, with women reporting mostly issues with sex drive, and men with sex drive and arousal. Symptoms of SD were found to be significantly correlated with older age, female gender, lower QoL and depressive symptoms, while no significant correlations were found with the type of epilepsy and the AEDs.

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**Conflict of interest:** None to declare.

## Contribution of individual authors:

Katarina Ivana Tudor - helped design the study and wrote the protocol, helped with collecting the data and contributed data or analysis tools, partially did statistical analyses, interpreted the results and wrote the manuscript.

Željka Petelin Gadže - organised the study and collection of the data, collected the data and contributed data or analysis tools, helped with interpretation of the results, and approved the final version of the manuscript.

Andreja Bujan Kovač, Monika Mudrovčić & Barbara Sitaš - collected the data, contributed data or analysis tools.

Ervina Bilić, Sandra Nađ Škegro, Mirko Bakula, Dinko Hauptman & Slavko Orešković - interpreted the results and approved the final version of the manuscript.

Sanja Hajnšek - conceived and helped design the protocol of this study.

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