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Abstract	Objectives Women with epilepsy (WWE) have special reproductive health needs. We compare menstrual disorders, obstetric outcomes, and patterns of contraceptive use among WWE in the reproductive age group to those without epilepsy. Methods Sixty WWE between the ages of 18 and 45 years were randomly selected from a hospital database, and 60 controls in the same age group were recruited from among their families or close contacts. A questionnaire adapted from the National Family Health Survey 5 (NFHS-5) was administered to collect data on menstrual patterns, obstetric outcomes, fertility preferences, and contraceptive use. Descriptive statistics were used. Graphical and cross-tabulations were used for comparisons. All statistics were performed on STATA version 14.2 (StataCorp, Texas, United States). Results The demographic characteristics including mean age, education, and occupational status were comparable. Dysmenorrhea requiring use of pain killers was more common among WWE (odds ratio [OR]: 3.01; 95% confidence interval [CI]: 1.11–8.72); other menstrual disorders were equally frequent. Spontaneous fetal loss was seen in 25 (21.9%) of 114 pregnancies in WWE and 22 (17.9%) of 123 among control women. Demand for family planning was satisfied in 21 (65.6%) of 32 eligible WWF and 23
	Demand for family planning was satisfied in 21 (65.6%) of 32 eligible WWE and 23 (62.2%) of 37 controls with the most common method being female sterilization. WWE knew fewer methods of contraception compared with controls (median: 2; interquar-
Keywords	tile range [IQR]: 1.2 vs. 4; IQR: 2.5; <i>p</i> < 0.0001).
 women with epilepsy menstrual disorder contraception 	Conclusion WWE had more dysmenorrhea and less knowledge of contraceptive methods compared with controls. Abnormal uterine bleeding, contraceptive use, and spontaneous fetal loss were similar in both groups.

Introduction

Epilepsy affects more than 2.73 million women in India, of whom over half are in the reproductive age group (15–49 years).¹ There are complex interactions among the hypotha-

article published online September 25, 2023 DOI https://doi.org/ 10.1055/s-0043-1772709. ISSN 2213-6320. lamic–endocrine axis, antiseizure medications (ASM), and the epileptic foci itself resulting in many reproductive health issues.² Women with epilepsy (WWE) are at increased risk of menstrual disorders like polycystic ovarian syndrome, spontaneous fetal loss, and congenital fetal malformations.^{3–5}

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Contraceptive advice for ensuring safe pregnancies among WWE, particularly with respect to hormonal contraceptive use, is challenging.⁶

However, the existing guidelines for management of WWE do not cover all important areas.^{7,8} One of the main reasons cited for this is the lack of context-specific evidence,^{8,9} including the prevalence and patterns of various reproductive health issues among the WWE. As reproductive health is a complex construct including many areas from sexuality to menopause, information regarding reproductive health is often obtained piecemeal and with variable definitions.^{9,10}

In India, most evidence on reproductive health of WWE revolves around pregnancy outcomes from the Kerala Registry of Epilepsy and Pregnancy (KREP). Information on menstrual disorders is incompletely characterized and often without adequate controls. Further, to the best of our knowledge, there is no information regarding contraceptive practices among WWE.¹⁰ In this study, we evaluate menstrual history, obstetric outcomes, and contraceptive use among WWE in the reproductive age group in comparison to control women without epilepsy.

Methods

Participants: This is a hospital-based study from a comprehensive epilepsy care center in South India. After obtaining ethical approval (JIP/IEC-OS/2022/149), we used the hospital electronic health records to retrieve a sampling frame of WWE between the ages of 18 and 45 years. We used random numbers to identify 60 participants. If we were unable to contact a participant or they were unwilling to participate, we replaced them with another participant from this list. Controls without epilepsy were recruited in the same age group from the family or close contacts of the WWE to roughly match the socioeconomic status and lifestyle of the WWE. Written informed consent was obtained from all participants. Women with significant disability (e.g., intellectual challenge) precluding their participation in the survey were excluded. Flow of participants is depicted in Fig. 1. Demographic details and epilepsy-specific details were collected, and all women were administered a questionnaire. The instrument was adapted from three sections of the National Family Health Survey-5 women's questionnaire, which is an open-source, culture-appropriate, closeended reproductive health survey available in local languages.¹¹ We supplemented this with additional questions from a tool used by Laksham et al to collect menstrual history in the urban population of Pondicherry.¹²

Sample size calculation: For a power of 80%, α of 0.05 and 1:1 matching assuming that more than a third of WWE (30%) have abnormal menstrual patterns, compared with 10% of normal women,¹³ we need to study 56 subjects in each arm.

Statistical methods: According to International Federation of Gynaecology and Obstetrics, abnormal uterine bleeding is defined in nonpregnant women as any abnormality of the menstrual cycle in terms of regularity, frequency, days of bleeding, or amount of bleeding.¹⁴ Spontaneous fetal loss defined the number of women experiencing any pregnancy



Fig. 1 Patient flow in the study.

loss due to spontaneous abortion, miscarriage, or still birth.⁵ Demand for family planning satisfied was defined as women living with their spouses and not wanting children and were using a modern contraceptive method. We estimated an odds ratio (OR) with 95% confidence interval (CI) for the occurrence of any menstrual disorder between the two groups. In addition, we used cross-tabulations to study the effect of ASMs (number of ASMs, types of ASM) on outcomes and odds ratios with confidence intervals, if appropriate, were estimated. All statistical analyses were performed at 5% level of significance using STATA version 14.2 (StataCorp, Texas, United States).

Results

The demographic details except for marital status (**-Table 1**) were comparable between both groups. Fifty-four (90%) WWE had epilepsy for 2 or more years. The details of epilepsy and antiseizure medications are listed in **-Table 1**.

Menstrual abnormalities: Abnormal uterine bleeding was seen in half the women in both groups (OR: 0.94; 95% CI: 0.43–2.03) and irregular cycles was the most common complaint (**-Table 2**). Seven women in each group were either pregnant or lactating at the time of interview. Four WWE had amenorrhea of greater than 6 months as against none in the control group. All these four women were in their late 30s and had no other reasons for the amenorrhea. Menstrual disorders interfering with work occurred in 11 (18.3%) in both groups, but that interfering with domestic responsibilities was more common among WWE (21 [35%]) than among controls (24 [40%]). Any pain during period was reported in almost all the women studied (109 [90.1%]), but

Demographic details	WWE (60)	Control (60)		
Age in years ^{a,b}	31.2 (6.9)	33.2 (6.8)		
Years of formal education				
Less than 8 years	15 (25%)	22 (36.7%)		
• 8 to 12	26 (43.3%)	35%)		
• More than 12	14 (23.3%)	17 (28.3%)		
Occupation				
Homemaker	39 (60%)	29 (48.3)		
Agriculture	11 (18.3%)	23.3%)		
Others	10 (16.6%)	17 (28.3%)		
Co-morbidities	7 ^c (11.7%)	2 ^d (3.3%)		
Marital status				
 Currently married 	41 (68.3%)	52 (86.7%)		
 Never married 	13 (21.7%)	6 (10%)		
 Separated or divorced 	6 (10%)	2(3.3%)		
 Age at marriage^a 	21.1 (4)	21.5 (4)		
Type of epilepsy				
• Focal	20 (42.5)			
 Generalized 	21 (44.7)			
 Unknown 	6 (13)			
Antiseizure medications				
• None	4 (6.7%)			
• 1	30 (50%)			
• 2 or more	26 (43.4%)			
Used as monotherapy or in combination				
Valproate	25 (41.6%)			
Carbamazepine	22 (36.7%)			
 Levetiracetam 	15 (25%)			

Table 1 Baseline characteristics of women with epilepsy (WWE) and controls

 Table 2 Menstrual history and reproductive outcomes of women with epilepsy (WWE) and controls

	WWE (60)	Control (60)	
Age (y) at menarche ^a	13.6 (1.4)	14.3 (1.4)	
Abnormal uterine bleeding	30 (50%)	31 (51.7%)	
 Irregular periods 	21 (35%)	16 (26.7%)	
• Excessive bleeding with passage of large clots	11 (18.3%)	13 (21.7%)	
 Intermenstrual interval >35 d 	3 (5%)	1 (1.6%)	
• Bleeding ≥7 d	5 (8.3%)	1 (1.6%)	
Amenorrhea >6 mo	4 (6.7%)	0	
Dysmenorrheal requiring painkillers	19 (31.7%)	8 (13.3%)	
Reproductive outcomes ^b			
 Number of pregnancies 	2 (1.3)	2 (1.3)	
• Number of abortions	0 (0.1)	0 (0.1)	
Number of live births	2 (1.2)	2 (1.2)	
Number of live children	1 (1.2)	1 (1.1)	

^aGiven as mean (standard deviation).

^bAs median (interquartile range); all others given as numbers (proportion).

Contraception: WWE knew a median of two (IQR: 1.2) methods of contraception compared with four (IQR: 2.5) among controls (p < 0.0001). Women knew about female sterilization (54 [90%] WWE vs. 60 [100%] controls), followed by intrauterine device (IUD) (38 [63.3%] WWE vs. 58 [96.7%] controls). Of 41 WWE currently married and living with their husbands, 27 (65.8%) reported ever having used a contraceptive compared with 30 of 52 women in the control group (57.7%). Thirty-two (78%) WWE and 37 (71.1%) controls did not want more children, were not pregnant, and the demand for family planning was satisfied in 21 (65.6%) WWE and 23 (62.2%) controls. Fig. 2 shows the methods used. The most common reasons for not using contraceptives were fear of side effects and lack of knowledge, while the most common reasons for discontinuing use of a contraceptive were desiring pregnancy and fear of side effects. Fewer WWE reported having been advised about the side effects of the contraceptives (8 [15.4%]) compared with controls (22 [44.2%]).

Discussion

We found that abnormal uterine bleeding was equally frequent between the two groups and there were no significant differences in the reproductive outcomes. The demand for family planning was satisfied in the majority of women in both groups. However, WWE had a significantly more severe dysmenorrhea and four WWE had amenorrhea for greater than 6 months. WWE were more likely to be single and had less knowledge of contraceptive methods.

Among 271 younger WWE from Poland (mean age of 29.6 years), the reported frequency of menstrual disorders was

^aGiven as mean years (standard deviation).

^bNo significant difference (p = 0.1); all others given as n (%).

^cTwo had mild intellectual disability, and one each had hypertension, diabetes mellitus, hypertension and diabetes mellitus, heart disease, and hypothyroid.

^dOne each with hypertension and diabetes mellitus.

dysmenorrhea requiring medications was more common in WWE (OR: 3.01; 95% CI: 1.11–8.72). There was no association of abnormal uterine bleeding with valproate use (OR: 0.87; 95% CI: 0.27–2.75).

Marital and reproductive outcomes: Fewer WWE were currently married (OR: 0.33; 95% CI: 0.11–0.90). The numbers of pregnancies, live births, and abortions were similar in both groups (**-Table 2**). Of 114 pregnancies in 45 WWE, 25 (21.9%) spontaneous losses were seen compared with 22 (17.9%) of 123 pregnancies in 51 controls. The median number of children wanted by the respondents was two (IQR: 2.2) in both groups, and most felt that their husband would want the same number (36 [87.8%] in WWE and 52 [96.3%] in controls).



Fig. 2 Type of contraceptive used among women with epilepsy and controls.

lower (28.8%). However, the authors did not clearly define menstrual disorders.¹⁵ A cross-sectional study of 380 WWE from Iran found 34.7% to suffer from irregular menstruation, similar to our finding.¹⁶ Among 427 Indian WWE, irregular cycle or prolonged cycle length was reported in 60 (14.1%) WWE,³ lower than our estimate. However, none of these studies had a control group and they all had variably defined menstrual disorders. We found abnormal uterine bleeding to be common and equally frequent in both women with and without epilepsy. These findings are similar to those reported from normal women in the reproductive age group in India,¹² and may reflect the shared environmental and possibly genetic factors due to the matching. We did not find any definite association between use of valproate and occurrence of abnormal uterine bleeding unlike previous reports.¹⁷ As the numbers of participants were small and use of valproate was common (25; 41.7%), in our study, we may not have been able to show this association. We found four (6.7%) WWE with amenorrhea for 6 months or more despite being aged less than 40 years. This probably indicates premature menopause. Other authors have reported similar occurrence among WWE.¹⁸ Menstrual pain requiring painkillers was significantly more common among WWE (OR: 3.01; 95% CI: 1.11-8.72), although any pain was similar to what was reported among normal women by Laksham et al.¹² No previous studies specifically reporting on dysmenorrhea among WWE are available.

Culturally marriage is nearly universal in India and our country reports the lowest divorce rates (1.1%). Our WWE were more often divorced (6%) and less likely to be currently married. Another study of 100 WWE from India similarly reported a higher divorce rate among WWE (8%).¹⁹ The relationship between higher divorce rates and epilepsy has been reported from other countries also.^{20–22} The increased rate of divorce is probably due to multiple factors, including epilepsy, its associated comorbidities, and psychosocial stigma. These factors also probably influence the likelihood of ever being

married as is seen in the larger proportion of never married WWE in our study (13 [21.7%] vs. 6 [10%]). Such a difference has also been observed by other authors from India.²³ In a review of marital problems among WWE in the South Asian setting, a compelling case for context-specific psychobehavioral research in this important area has been put forth.²⁴

We found a numerically higher proportion of spontaneous fetal loss among our WWE, but this difference was not statistically significant. Data from the National Family Health survey-3 suggest the rate of spontaneous fetal loss is around 14%,²⁵ which is similar to our finding. However, data from the KREP registry suggest spontaneous fetal loss among WWE to be lower than that in our study (6.9%).⁵ This lower rate is likely due to the differences in methods used to ascertain fetal loss and may also be reflective of the better health indices in the state of Kerala, India.

Contraception for WWE is a complicated decision requiring consideration of the nature of epilepsy, contraceptive needs, and drug interactions.²⁶ The majority of WWE and controls in our study used female sterilization to meet their contraceptive needs, similar to the rest of the country.²⁷ However, unlike the national level data where condoms (11.8%) and oral contraceptive pills (8.5%) were also used by a significant proportion, fewer women in our study in either group used these (pills: 0 and condoms: 4 [3.8%]). This may be due to regional variations in contraceptive practices, and smaller numbers in our study. Around a third of eligible WWE did not use an effective contraceptive. This is similar to Western data, where a crosssectional survey of 1,144 WWE found that only 70% of eligible WWE used a highly effective method of contraception.²⁸ This study also reported that the most common contraceptive used was systemic hormonal contraceptives (46.6%) followed by barrier methods (23.2%), while only 4% used female sterilization unlike our WWE.²⁹ These low rates of contraceptive utilization in both settings are indeed worrisome as planned pregnancy in WWE is essential to ensure optimal outcomes for the mother and baby.

Knowledge of contraceptive methods was found to be lower among WWE compared with controls. This is despite our WWE having similar level of educational and more health care contact compared with the controls. We hypothesize that this discrepancy is likely to due to lack of structured discussion around reproductive health during routine clinical encounters with WWE. Such poor counseling of WWE regarding contraception is a well-recognized problem worldwide and needs to be addressed.^{10,26,30,31}

Our study has certain strengths. We adopted most of the survey items from the National Family Health Survey, a standardized instrument that has been used to measure reproductive health across our country. We had a control group of women, who were identified by WWE from among their family members or close contacts, thus controlling for socioeconomic and possibly environmental confounders. This enabled us to understand the reproductive health of WWE in the correct context. However, our sample of WWE was hospital based, and was not adequately powered due to a difference in the assumed prevalence of menstrual disorders and the actual estimate. We used a survey methodology, which has its own inherent biases.

Conclusion

While it appears that our WWE had similar abnormal uterine bleeding, contraceptive use, and spontaneous fetal loss as our control group, WWE had more dysmenorrhea, were less likely to be married, and had less knowledge of contraceptive methods compared with controls. More long-term prospective studies using a life course approach are needed to adequately reflect the reproductive health of our WWE. Urgent measures are needed to ensure adequate contraceptive counseling for WWE as contraceptive choices are complicated by epilepsy and planned pregnancy is of utmost importance for WWE.

Ethical Approval

This study was approved by the institutional ethics board (JIP/IEC-OS/2022/149).

Data Availability Statement Data are available on request from the authors.

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Conflict of Interest None declared.

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