

Reproductive Dysfunction in Epileptic Females

Tarek Desoky^a, Yasmine Mohammed Ahmed^{a*}, Mahmod Sliman Iwus^b, Mohamed Moslem Hefny^a, Ahmed Fathi Zaki^a

^aDepartment of Neuropsychiatry, Faculty of Medicine, South Valley University, Qena, Egypt.

^bDepartment of Obstetrics and Gynecology, Faculty of Medicine, South Valley University, Qena, Egypt.

Abstract

Background: Epilepsy is one of the most serious neurological disorders characterized by recurrent fits and has a lot of comorbidities. Epileptic females have reproductive dysfunctions due to epilepsy itself and use of antiepileptic drugs (AED).

Objectives: to early detection and treatment of reproductive complications in epileptic female.

Patients and methods: This is a cross-sectional study, was done on 40 epileptic female patients at neurology department outpatient clinic Qena University Hospital.

Results: Forty epileptic women in reproductive age were included in the study, the mean age was 27.05 ± 5.354 years with mean age of menarche 13 ± 1.641 years. Mean age of onset of fits was 20 ± 5.914 years. 25% of women have a reproductive problem in form of PCOS and 37.5% have an irregular menstrual cycle.

Conclusion: Epilepsy and antiepileptic drugs may affect reproductive functions in epileptic females

Keywords: Antiepileptic Drugs; Epileptic Females; Reproductive Dysfunctions.

DOI: 10.21608/SVUIJM.2023.192251.1518

***Correspondence:** yassminemohammed@gmail.com

Received: 1 February, 2023.

Revised: 19 February, 2023.

Accepted: 27 February, 2023.

Published: 11 January, 2025

Cite this article as: El Sayed Said, Mohammed Fathy Amin, Hossam Ahmed Attya, Mohamed El-Sayed Anwar Kenawy.(2024). Management of Length Unstable Pediatric Femoral Fracture by Elastic Nails. *SVU-International Journal of Medical Sciences*. Vol.7, Issue 2, pp: 1083-1088.

Copyright: © Desoky et al (2024) Immediate open access to its content on the principle that making research freely available to the public supports a greater global exchange of knowledge. Users have the right to Read, download, copy, distribute, print or share link to the full texts under a [Creative Commons BY-NC-SA 4.0 International License](https://creativecommons.org/licenses/by-nc-sa/4.0/)

Introduction

Epilepsy, drugs that control seizures and reproductive system have complex interactions. Women with epilepsy (WWE) have lower fertility than general population due to epilepsy and AED (Weber et al., 2006).

The use of liver enzyme inducer antiepileptic drugs (AED) affect the activity of testosterone and estradiol leading to menstrual abnormalities and thus to infertility (Kaaja et al., 2002). The use of sodium valproate associated with polycystic ovaries (PCO) and menstrual irregularities (Vajda et al., 2008). The use of transvaginal u/s and assessment of testosterone level are helpful to detect the reproductive dysfunctions due to use of sodium valproate. (Artama et al., 2006).

Use of liver enzyme inducers AED increase metabolism of combined oral contraceptive pills (COCs) leading to unplanned pregnancy also use of oral contraceptive pills affects the level of some drugs as lamotrigine leading to uncontrolled fits (Coulam 1989).

Patients and methods

This study was a descriptive cross-sectional study which was done in Neurology Department Qena University Hospital.

a. Inclusion criteria: Forty epileptic females between (13-40) years old on monotherapy of AED.

b. Exclusion criteria: Reproductive complications due to another medical condition, other major psychiatric illness or use of antipsychotic and antidepressant drugs.

Study methods

Full history (personal history, neurological history, and menstrual history), general examination, Body mass index (BMI). Full neurological examination

Investigations

Radiographic investigation (trans vaginal and trans abdominal u/s). Laboratory (FSH/LH and prolactin level)

Informed written consent was obtained from all participants. The Ethics Committee of faculty of Medicine, South Valley University, Egypt approved the study (ethical code 473).

Statistical analysis

SPSS version 21.0 program was used for analysis and processing of data. Tables used to prepare data as mean values \pm standard deviations (SD) and compared by student t-test. Values considered significant if P values equal or less than 0.05.

Results

Demographic data in studied group

A number 40 epileptic women in reproductive age were included in the study; the mean age was 27.05 ± 5.35 years with mean age of menarche 13 ± 1.64 years. mean age of onset of fits was 20 ± 5.91 years. As shown in (Figs.1,2) from the total number of studied women, 25% of women have a reproductive problem in form of PCOS and 37.5% have an irregular menstrual cycle. Details of demographic and reproductive problems of the women are presented in (Tables.1,2, Figs.1,2).

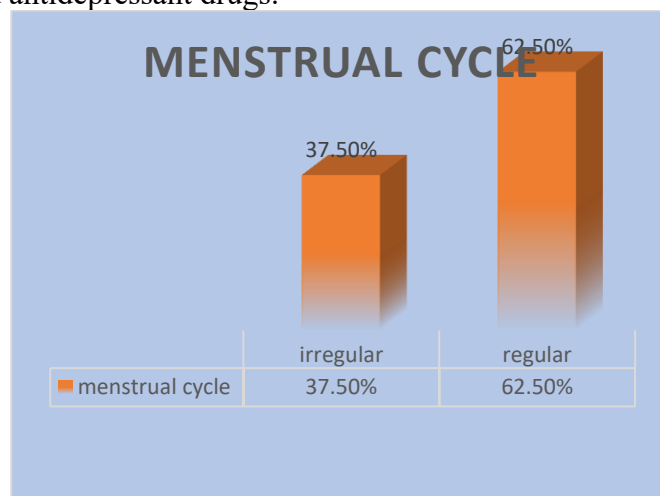


Fig.1. Percentage frequencies of menstrual cycle irregularity in the studied women

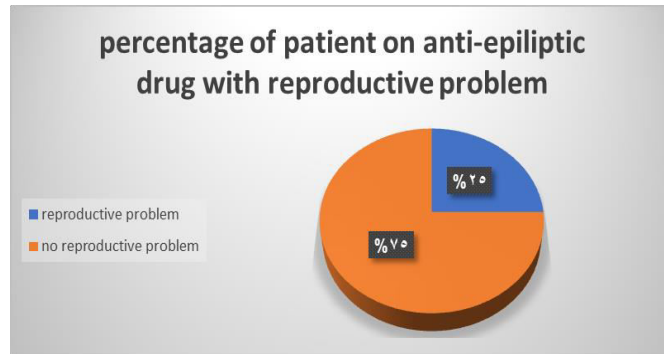


Fig.2. Percentage frequencies of patients with reproductive problem and on anti-epileptic drugs

Table 1. Demographic data in studied group

Characteristics	Mean + Std. DEVIATION
Age of menarche (N=40)	13 +1.641
Age of women in the study(N=40)	27.05+5.354
Age of onset of fits (N=40)	20+5.914
duration of using of anti-epileptic drug(N=40)	5.8+ 2.857

Table2. Reproductive characteristics of the studied women (n=40)

Reproductive function characteristics	NO	%
Reproductive problem in form of PCOS(N=40)		
•Yes	10	25
•NO	30	75
Menstrual cycle regularity (N=40)		
•Regular	25	62.5
•Irregular	15	37.5

Diagnosis of PCOS through laboratory investigation and ultrasound picture of pco among studied women

From the total number of studied women ,22.5%of women have a picture of PCO in

ultrasound. Mean of FSH, LH and Prolactin hormone are 6.5 ± 1.05 , 9.22 ± 3.25 and 13.65 ± 3.45 (p-value <0.05) as shown in (Tables.3,4).

Table 3. Ultrasound picture of PCO among studied women

Ultrasound picture of PCO	Percentage(N)
• Normal	77.5% (31)
• Picture of PCO	22.5% (9)

Table4. Diagnosis of PCOS through laboratory investigation

FSH	6.500+1.0500
• Mean+ SD	
LH	9.225+3.2511
•Mean+ SD	
Prolactin	13.65+3.453
•Mean+ SD	
Body Mass Index	20.40+2.649
•Mean+ SD	

Relationship between reproductive problem and anti-epileptics drug use, compliance of treatment and control of fits

There is a strong statistically significant relation between type of anti-epileptic drug uses and to have a reproductive problem in form of PCOS ($P < 0.0001$) as shown in table 8. 25% of total females in the study and have a

reproductive problem and use sodium valproate which indicate that sodium valproate is the most anti-epileptic drug involved in reproductive problem in form of PCOS. There is no significant relation between compliance on treatment or control of fits and having a PCOS ($P = 0.251$ as shown in (Table.5).

Table5. Percentage of different type of anti-epileptics drugs used by females shared in the study, compliance on treatment -and control of fits .

Variables	Reproductive problem (no)		Reproductive problem (yes)		P value
	No	%	No	%	
Depakin	2	5%	10	25%	<0.0001**
Livetracetam	10	25%	0	0%	<0.0001**
tegetrol	10	25%	0	0%	<0.0001**
lamotrigine	8	20%	0	0%	<0.0001**
Compliance on ttt	18	45%	8	20%	0.251
Non compliance	12	30%	2	5%	0.251
Controlled fits	18	45%	8	20%	0.251
Partially controlled	12	30%	2	5%	0.251

Discussion

In the present study, a total of 40 women on anti-epileptic drugs and in reproductive age were included in the study, the mean age was 27.05 ± 5.354 years with mean age of menarche 13 ± 1.641 years. The age of onset of fits was 20 ± 5.914 years. In this study there was a total number of studied women, 25% of women have a reproductive problem in form of PCOS and 37.5% had an irregular menstrual cycle.

This can be supported by (Tao et al.,2018) who conducted a case control study on 112 epileptic female and 120 normal controls. The study reported that the mean age of epileptic females ($N = 112$) between the age of 20 and 50 years, with mean age of 35.03 ± 10.17 years. The epileptic females had higher infertility rates (33.0% vs 6.7%) and menstrual irregularities (39.3% vs 20.8%) in comparison with the healthy group.

Also, the study by (Ogunjimi et al., 2021) enrolled 100 WWE with mean age 29.07 ± 7.55 years, the study reported that the incidence of 30% of PCOS. The frequency of

PCOS was significant in the epileptic females group compare to the healthy group.

However, (Hamed et al.,2007) reported increase in the rate of cycle abnormalities in 71.6% of epileptic females compared to 21.7% of control group . the most common was oligomenorrhea (90.4%) while amenorrhea and menorrhagia was about 19.2% and 11.5%.

As previously mentioned, the rate of infertility in epileptic females is 38.4%, which is two-fold higher than that healthy women .

In this current study we found that from the total number of studied women, 22.5% of women have a picture of PCO in ultrasound. Mean of FSH, LH and Prolactin hormone are 6.5 ± 1.05 , 9.225 ± 3.2511 and 13.65 ± 3.453 (p-value < 0.05). mean body mass index between epileptic female of participant women is 20.40 ± 2.649 (p-value < 0.0001) most of participant women were overweight.

In agreement with the current study (Osalusi et al., 2021) revealed that in the pre-ovulatory phase, WWE had lower FSH levels (5.8 mIU/ml; IQR: 3.2 - 11.7 mIU/ml) than

controls. Controls had similar LH/FSH ratio with WWE on medication. There was no significant difference in LH levels, estrogen, progesterone E/P ratio between females with or without treatment.

Also, (Ogunjimi et al.,2021) reported that women used carbamazepine(CBZ) FSH mean in the follicular was 10.87 ± 14.74 IU/L compared to 8.15 ± 12.31 IU/L between those used levetiracetam (LEV) and 4.56 ± 3.29 IU/L between healthy group, which had a level of significant difference between patients used treatment and the healthy group with a P value of (.021. In women on CBZ ,the luteal phase LH mean value was 12.50 ± 13.74 IU/L compared with mean value of 5.34 ± 3.24 IU/L between females on LEV and mean value of 7.26 ± 15.40 IU/L in normal group , which showed a significant difference in both groups with a P value of (.010) finally, testosterone mean value was higher in the groups used CBZ and levetiracetam .The mean BMI between epileptic females was 24.05 ± 4.18 .

The current study showed that 30% of participant women use sodium valproate while 25% use livetracetam and only 20% use lamotrigine. 65% of participants were compliance on treatment and have controlled fits.

However, the study by (Tao et al.,2018) reported that 112 patients used AEDs. 61 patients were on monotherapy, including 12 used lamotrigine (LTG), 8 on carbamazepine (CBZ), 12 with on oxcarbazepine (OXC), 7 used valproate (VPA), 18 treated with levetiracetam (LEV), and 4 with topiramate (TPM). In all, 33 patients used two AEDs, while 18 were on triple therapy or more AEDs. While Razaz et al., reported that Lamotrigine (628 [46.1%]) and carbamazepine (418 [30.7%]) were the most commonly used AEDs, and 181 infants (13.3%) were exposed to polytherapy. The treatment may vary from study to another depending on the type and severity of Epilepsy.

In the current study there is a strong relation between type of anti-epileptic drug

used and reproductive problem in form of PCOS (P <.0001). Results showed that 25% of total females in the study and used sodium valproate had reproductive problem which indicate that is the most anti-epileptic drug involved in reproductive problem in form of PCOS. There is no relation between compliance on treatment or control of fits and having a PCOS(P =0.251).

This can be supported by (Osalusi et al., 2021) who reported that there was a significant relation between the use of anti-epileptic drugs and reproductive problem women.

Also, the review by (Menon et al.,2019) showed that there was a significant relation between the use of anti-epileptic drugs and the improvement of reproductive health in women. Furthermore, (Sukumaran et al., 2010) reported that the use of multiple AEDs was a significant predictor of infertility in women. However, (Tao et al 2018. reported that reported that there was no significant relation between the use of anti-epileptic drugs and sexual health problem women.

Conclusion

Women with epilepsy had low FSH, LH hormones and mostly overweight. We also found that reproductive problems in form of pco were significantly associated with type of AEDs mostly sodium valproate ,compliance on treatment and control of fits. Further studies with more sample size are needed to support our primary results and to assess the side-effects associated with the use of AEDs.

References

- **Artama M, Isojärvi J, Auvinen A. (2006).** Antiepileptic drug use and birth rate in patients with epilepsy--a population-based cohort study in Finland. *Human reproduction* (Oxford, England), 21(9): 2290–2295.
- **Coulam C B, Annegers JF .(1979).** Do anticonvulsants reduce the efficacy of oral contraceptives?. *Epilepsia*, 20(5): 519–525.
- **Hamed S A, Hamed E A, Shokry M, Omar H, Abdellah M M .(2007).** The reproductive conditions and lipid profile in females with epilepsy. *Acta neurologica Scandinavica*, 115(1): 12–22.

- **Kaaja E, Kaaja R, Matila R, Hiilesmaa V.(2002).** Enzyme-inducing antiepileptic drugs in pregnancy and the risk of bleeding in the neonate. *Neurology*, 58(4):549–553.
- **Mattson R H, Cramer J A, Darney P D, Naftolin F .(1986).** Use of oral contraceptives by women with epilepsy. *JAMA*, 256(2): 238–240.
- **Menon S, Siewe Fodjo J N, Weckhuysen S, Bhwana D, Njamnshi A K, Dekker M, et al. (2019).** Women with epilepsy in sub-Saharan Africa: A review of the reproductive health challenges and perspectives for management. *Seizure*, 71: 312–317.
- **Ogunjimi L, Yaria J, Makanjuola A, Alabi A, Osalusi B, Oboh D, et al.(2021).** Polycystic ovarian syndrome in Nigerian women with epilepsy on carbamazepine/levetiracetam monotherapy. *Acta neurologica Scandinavica*, 143(2): 146–153.,
- **Osalusi BS, Ogunjimi L, Yaria J, , Ale A, Ogunsemi O, Akinyinka A, et al.(2020).** . Thehormonal Changes Among Nigerian Women With Epilepsy. *African Journal Of Science And Nature*,10(10):32-8.
- **Razaz N, Tomson T, Wikström A K, Cnattingius S .(2017).** Association Between Pregnancy and Perinatal Outcomes Among Women With Epilepsy. *JAMA neurology*, 74(8): 983–991.
- **Roberts JI, Metcalfe A, Abdulla F, Wiebe S, Hanson A, Federico P, et al .(2011).** Neurologists' and neurology residents' knowledge of issues related to pregnancy for women with epilepsy. *Epilepsy & behavior : E&B*, 22(2): 358–363.
- **Sukumaran S C, Sarma P S, Thomas S V .(2010).** Polytherapy increases the risk of infertility in women with epilepsy. *Neurology*, 75(15): 1351–1355.
- **Tao, L, Zhang X, Duan Z, Wang Y, Liu J, Hou H, et al. (2018).** Sexual dysfunction and associated factors in Chinese Han women with epilepsy. *Epilepsy & behavior : E&B*, 85: 150–156.
- **Vajda F J, Hitchcock A, Graham J, O'Brien T, Lander C, Eadie M .(2008).** Seizure control in antiepileptic drug-treated pregnancy. *Epilepsia*, 49(1): 172–176.
- **Webber M P, Hauser W A, Ottman R, Annegers J F. (1986).** Fertility in persons with epilepsy: 1935-1974. *Epilepsia*, 27(6). 746–752.