

ORIGINAL ARTICLE

Fits in Pregnant Women with Previously Controlled Epilepsy: A Cross Sectional Study

SAFIA GUL¹, IMRAN KHAWAJA², ASIYA GUL³, ASAD KHAWAJA⁴, ALI BASHARAT⁵¹Medical Officer Obs and Gyne department, Ayub Teaching Hospital, Abbottabad²Senior Registrar Medicine, Ayub Teaching Hospital, Abbottabad³Medical Officer Obs and Gyne department, Holy Family Hospital, Rawalpindi^{4,5}House Officer, Ayub Teaching Hospital, AbbottabadCorresponding author: Imran Khawaja, Email: dr.imran239@gmail.com, Cell: +923348963956

ABSTRACT

Background and Aim: Pregnant women with epilepsy require stability in maternal fits and antiepileptic drugs have potentially adverse effects in developing fetuses. Hypoxemia and blunt trauma cause convulsive fits which are treacherous to both maternal and fetus. Limited data available regarding frequency of fits in pregnant women with previously controlled epilepsy. The present study was carried out to evaluate the frequency of fits in pregnant women with previously controlled epilepsy.

Methodology: This cross-sectional study was conducted on 70 pregnant women with a previous history of epilepsy in the Department of Obstetrics and Gynecology, Ayub Teaching Hospital, Abbottabad and Holy Family Hospital, Rawalpindi from January 2021 to December 2021. The incidence of Fits during pregnancy was compared through a peripartum period (epoch 1) and during the postpartum period (epoch 2). Non-pregnant epilepsy women were enrolled as controls and were followed for 18 months period. A higher frequency of Fits was the prime outcome in epoch 1 compared to epoch 2. Administered drugs such as antiepileptic drugs doses were compared.

Results: A total of 70 pregnant and 60 controls women with epilepsy were enrolled. Out of 70, about 60 had a history of previous fits or Fits. The prevalence of fits was significantly higher during epoch 1 whereas in epoch 2, about 21% had Fits and 23% in control had Fits (Odd ratio: 0.89; 95% CI: 0.49-1.57). Of those 60, 22 (36.7%) of the pregnant subjects recruited had a history of eclampsia-related fits. An antiepileptic drug dose during pregnancy was changed in 69% of pregnant women and 29% in control (odd ratios; 6.41; 95% CI, 3.79-10.63).

Conclusion: Our study found that the percentage of epilepsy diagnosed women had a higher frequency of fits during pregnancy compared to the postpartum period was comparable to the control group (non-pregnant) women. During comparable time periods, pregnant women experienced more changes in antiepileptic drug doses than non-pregnant women.

Keywords: Fits, epilepsy, pregnancy

INTRODUCTION

Epilepsy is a common and serious neurological condition characterized by a persistent proclivity to produce epileptic fits with neurobiologic, cognitive, and psychosocial consequences [1,2]. In developed countries, the annual incidence of epilepsy is approximately 50–70 cases per 100,000 population, with a prevalence of approximately 5–10 per 1000. With an incidence of 100–190 cases per 100,000 people per year [3,] the developing world accounts for a large proportion of cases. Pregnant women with epilepsy require stability in maternal fits or fits and antiepileptic drugs have potentially adverse effects in developing fetuses. Hypoxemia and blunt trauma cause convulsive fits which are treacherous to both maternal and fetus [4]. Several studies have found that pregnant women with epilepsy have a higher rate of maternal death than other pregnant women, with up to 79% of epilepsy-related deaths attributed to sudden, unexpected death. [5, 6] The prevalence of increased fits frequency among women during pregnancy ranges from 14 to 62%. [7, 8].

During pregnancy, women diagnosed with epilepsy are considered to be susceptible to higher risk of complications [9], despite previous research showing no significant increase in fits burden during pregnancy [10]. When compared to the non-epileptic group, epilepsy diagnosed women had higher prevalence of cesarean section, vaginal bleeding, premature delivery, and pre-

eclampsia [11], while few others studies reported insignificant increased in neonatal and perinatal complications [12]. Convulsive fits are hazardous to both the mother and the fetus due to blunt trauma and hypoxia. The management of epilepsy during pregnancy necessitates balancing maternal fits control with the teratogenic and neurocognitive risks to the fetus [13]. Teratogenic potential and associated risks vary greatly among ASDs (anti-fits drug). The majority of fits during pregnancy occur in women who already have epilepsy. Fits with new onset are a complication of eclampsia; however, in rare cases, women develop epileptic fits with new onset during pregnancy [14]. Fits that occur during pregnancy (in the absence of eclampsia) may be triggered by stress, sleep deprivation, and hormonal changes. The present study was conducted to evaluate the frequency of fits in pregnant women with controlled epilepsy.

METHODOLOGY

This cross-sectional study was conducted on 70 pregnant women with a previous history of epilepsy in the Department of Obstetrics and Gynecology, Ayub Teaching Hospital, Abbottabad from January 2021 to December 2021. The prevalence of Fits or fits during pregnancy was compared through a peripartum period (epoch 1) and during the postpartum period (epoch 2). Non-pregnant epilepsy women were enrolled as controls and were

followed for 18 months period. A higher frequency of Fits was the prime outcome in epoch 1 compared to epoch 2. Administrated drugs such as antiepileptic drugs doses were compared. Exclusion criteria for the two groups include an expectation that the patient would have a difficult-to-measure or significantly altered frequency of fits (e.g., the presence of progressive cerebral disease, planned surgical intervention for epilepsy, a history of psychogenic nonepileptic fits, or drug or alcohol abuse in the previous year) or features that were expected to alter other primary outcomes of the study (e.g., >20 weeks of gestation in the pregnant group, or drug or alcohol abuse in the previous year).

We conducted study visits for pregnant women three times during pregnancy, once during labour and delivery, and once every three months through nine months after delivery (total evaluation period, 18 months). Women in the control group went to the same number of appointments as pregnant women. To improve recruitment, gestational age was calculated based on the estimated due date, and the first study visit could be scheduled up to 20 weeks of gestation. Visits were scheduled between 21 and 27 weeks and 30 and 36 weeks during the second and third trimesters, respectively. When the first visit occurred during the second trimester, the next visit was at least four weeks apart. The prime consequence was the women proportion who had more fits that impair awareness in epoch 1 compared to epoch 2. The percentages of women with this outcome in the two groups were then compared. Despite the fact that all fits types were investigated, fits that impaired awareness were chosen as the primary outcome due to their potential for negative clinical consequences. For the time periods studied, the frequency of fits was normalized to a 28-day rate.

Secondary outcomes included the proportion of women with an increased fits frequency in each trimester and peripartum period, the proportion of women who had an increased frequency of other fits types, the percentage who had a change in antiepileptic drug dose during pregnancy, the within-person change in the 28-day incidence of fits, and the proportion of women who had fits or convulsions during epoch 1 among those who were fits-free or convulsive. To summarize the results of all outcomes, including the primary outcome, we calculated the percentage of women who had an increased frequency of fits (along with 95 percent confidence intervals) in epoch 1 compared to epoch 2. For between-group comparisons, we calculated odds ratios and 95 percent confidence intervals from logistic-regression models for each fits type.

RESULTS

A total of 70 pregnant and 60 controls women with epilepsy were enrolled. Out of 70, about 60 had a history of previous fits or Fits. The prevalence of fits was significantly higher during epoch 1 whereas in epoch 2, about 21% had Fits and 23% in control had Fits (Odd ratio: 0.89; 95% CI: 0.49-1.57). Of those 232, 86 (37.1%) of the pregnant subjects recruited had a history of eclampsia-related fits. An antiepileptic drug dose during pregnancy was changed in 69% of pregnant women and 29% in control (odd ratios; 6.41; 95% CI, 3.79-10.63). Participants' Baseline Characteristics is shown in Table-1. Table-II demonstrate

the primary outcomes and secondary outcomes based on timing whereas Figure-1 illustrate the primary outcomes based on fits different types. Variations in fits frequency among pregnant women are shown in Figure-2.

Table 1: Participants' Baseline Characteristics

Parameters	Pregnant Women (n=70)	Control (n=60)
Age (years)	29±4.5	31±6.5
Education		
High school	19 (27.8%)	18 (30.4%)
College or advance degree	51 (72.2%)	42 (69.6%)
Fits Types		
Generalized	20 (28.5%)	14 (22.5%)
Focal	48 (68.7%)	36 (59.8%)
Unclassified	2 (2.8%)	11 (17.6%)

Table 2: Primary and secondary outcomes

Outcomes	Pregnant Women with Outcomes n (%)	Control with Outcomes n (%)	Odds ratio 95% CI
Primary Outcomes			
Fits frequency during epoch 1 than during epoch 2	16 (22.9%)	15 (25%)	0.89 (0.49-1.57)
Secondary Outcomes (Weeks)			
First trimester (<13)	6 (8.6%)	8 (13.3%)	0.41 (0.11-1.54)
Second trimester (14-28)	12 (17.1%)	9 (15%)	0.79 (0.42-1.61)
Third trimester (>29)	11 (15.7%)	8 (13.3%)	1.17 (0.52-2.49)
Peripartum (6 wk after birth)	41 (58.6%)	35 (58.3%)	1.56 (0.67-3.79)

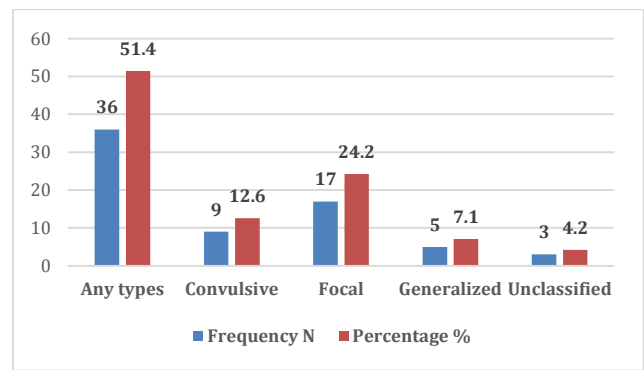


Figure 1: primary outcomes based on fits different types in pregnant women.

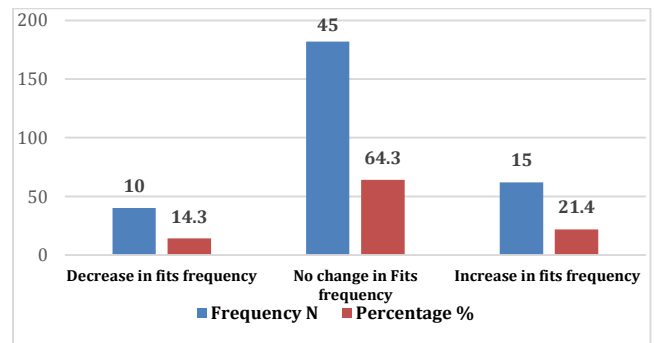


Figure 2: Variations in fits frequency among pregnant women

DISCUSSION

The present study found that no significant difference was there among pregnant and non-pregnant women in terms of fits frequency in epoch 1 against epoch 2. However, drug dose frequency was higher in pregnant women as compared to the control group. Fit frequency decreased by 14.3% and 21.4% increase in pregnant women. According to previous studies fits frequency increases during peripartum or certain trimester during pregnancy [15, 16]. However, in the current study no significant difference among the pregnant and control groups. Secondary outcomes illustrated that women with no fits before 9 months of pregnancy were more likely to continue fits-free during pregnancy compared to those who had fits that resembled previous studies [17]. Higher prevalence of fits were found in epilepsy diagnosed women during pregnancy that impaired awareness in postpartum period that resembled with women of control group or non-pregnant women during respective epochs [18].

Primiparas were present in majority of patients and their abortion imitated the disease concerns and possible effect on neonates and ASM adverse effects. More than half had an education of college or advance degree with stable social stable [19]. According to previous study, the design of variation is indistinct due to variation in fits frequency and no specific proof of increase or decrease burden on fits [20]. The study also found that fits frequency increase with mid-trimester and appears to be more obvious in other stages. Tonic-clonic fits were present in majority of patients before pregnancy and their occurrence increased to quarter stage of mid-trimester and completed at the pregnancy end. Another study discovered that convulsive fits are less common in pregnancy second half stage compared to first phases [21].

In contrast, we compared fits frequency changes by trimester in this study and found no decrease in advanced pregnancy, nor was associated with Lamotrigine and polytherapy influence. This could be caused by hormonal variations or changes in drug concentrations. As a result, larger-scale studies with a greater number of patients are required to validate the fits frequency changes during pregnancy [22]. Active epilepsy with better fits control has been the key focused of the current investigations [23].

Although a control group was present, but obstetric complications such as hypothyroidism, vaginal bleeding, pre-eclampsia, and anemia were common in this small sample during all trimesters. These hitches have previously been testified in pregnant women with active epilepsy. Particularly medications users during pregnancy [24]. The odds ratio for being fits-free during the 9 months before pregnancy or enrollment was 0.21 in risk-factor models that calculated a higher frequency of fits in epoch 1 than in epoch 2. (9% CI, 0.10 to 0.39).

Previous research has suggested that fits may increase during certain trimesters of pregnancy or during the peri-partum period [25-27], but we found no differences in pregnancy stage or fits type, including convulsive fits, between pregnant women and controls. Secondary outcomes revealed that women who had no fits in the 9 months preceding pregnancy or enrollment were more likely to remain fits-free during pregnancy than those who

had such fits, findings that were consistent with previous research. [28].

CONCLUSION

Our study found that the percentage of epilepsy diagnosed women had a higher frequency of fits during pregnancy compared to the postpartum period was comparable to the control group (non-pregnant) women. During comparable time periods, pregnant women experienced more changes in antiepileptic drug doses than non-pregnant women.

REFERENCES

1. AlSheikh MH. Prevalence of epilepsy in Saudi pregnant women and possible effects of anti-epileptic drugs on pregnancy outcomes. *Neurosciences Journal*. 2020 Jan 1;25(1):32-7.
2. Shahla M, Hijran B, Sharif M. The course of epilepsy and seizure control in pregnant women. *ActaNeurologicaBelgica*. 2018 Sep;118(3):459-64.
3. Sharma A, Gupta V, Sarda P, Singh P, Gupta N, Kohli S. Seizure disorders in pregnancy: an insight beyond eclampsia and epilepsy. *International Journal of Reproduction, Contraception, Obstetrics and Gynecology*. 2021 Nov 1;10(11):4201-6.
4. Pennell PB, French JA, Harden CL, et al. Fertility and birth outcomes in women with epilepsy seeking pregnancy. *JAMA Neurol*. 2018;75(8):962–969. doi:10.1001/jamaneurol.2018.0646
5. MacEachern DB, Mandle HB, Herzog AG. Infertility, impaired fecundity, and live birth/pregnancy ratio in women with epilepsy in the USA: findings of the Epilepsy Birth Control Registry. *Epilepsia*. 2019;60(9):1993–1998. doi:10.1111/epi.16312
6. Johnson EL, Burke AE, Wang A, et al. Unintended pregnancy, prenatal care, newborn outcomes, and breastfeeding in women with epilepsy. *Neurology*. 2018;91(11):e1031–e1039.
7. Herzog AG, Mandle HB, Cahill KE, et al. Predictors of unintended pregnancy in women with epilepsy. *Neurology*. 2017;88(8):728–733. doi:10.1212/WNL.0000000000003637
8. Mohllajee AP, Curtis KM, Morrow B, Marchbanks PA. Pregnancy intention and its relationship to birth and maternal outcomes. *ObstetGynecol*. 2018;109(3):678–686. doi:10.1097/01.AOG.0000255666.78427.c5
9. Herzog AG, Mandle HB, MacEachern DB. Association of unintended pregnancy with spontaneous fetal loss in women with epilepsy: findings of the epilepsy birth control registry. *JAMA Neurol*. 2019;76(1):50–55. doi:10.1001/jamaneurol.2018.3089
10. Sundaram A, Vaughan B, Kost K, et al. Contraceptive failure in the United States: estimates from the 2006-2010 National Survey of Family Growth. *Perspect Sex Reprod Health*. 2017;49(1):7–16. doi:10.1363/psrh.12017
11. Stephen LJ, Harden C, Tomson T, Brodie MJ. Management of epilepsy in women. *Lancet Neurol*. 2019;18(5):481–491. doi:10.1016/S1474-4422(18)30495-2
12. Edey S, Moran N, Nashif L. SUDEP and epilepsy-related mortality in pregnancy. *Epilepsia*. 2017;55(7):e72–e74. doi:10.1111/epi.12621
13. Viale L, Allotey J, Cheong-See F, et al. Epilepsy in pregnancy and reproductive outcomes: a systematic review and meta-analysis. *Lancet*. 2018;386(10006):1845–1852. doi:10.1016/S0140-6736(15)00045-8
14. Pennell PB, French JA, May RC, et al. Changes in seizure frequency and antiepileptic therapy during pregnancy. *N Engl J Med*. 2020;383(26):2547–2556. doi:10.1056/NEJMoa2008663

15. Quinlan JD, Murphy NJ. Cesarean delivery: counseling issues and complication management. *Am Fam Physician* 2015;91(3):178–184.
16. Soontornpun A, Choovanichvong T, Tongsong T. Pregnancy outcomes among women with epilepsy: a retrospective cohort study. *Epilepsy Behav* 2018;82:52–56. doi:10.1016/j.yebeh.2018.03.001
17. He S, Zhu H, Qiu X, et al. Pregnancy outcome in women with epilepsy in Western China: a prospective hospital based study. *Epilepsy Behav* 2017;74:10–14. doi:10.1016/j.yebeh.2017.05.034
18. Artama M, Braumann J, Raitanen J, et al. Women treated for epilepsy during pregnancy: outcomes from a nationwide population-based cohort study. *ActaObstetGynecolScand* 2017;96(7):812–820. doi:10.1111/aogs.13109
19. Allotey J, Aroyo-Manzano D, Lopez P, et al. Global variation in pregnancy complications in women with epilepsy: a meta-analysis. *Eur J ObstetGynecolReprodBiol* 2017;215:12–19. doi:10.1016/j.ejogrb.2017.05.016
20. Farmen AH, Grundt JH, Nakling JO, et al. Increased rate of acute caesarean sections in women with epilepsy: results from the Oppland Perinatal Database in Norway. *Eur J Neurol* 2019;26(4):617–623. doi:10.1111/ene.13865
21. Tomson T, Battino D, Bromley R, et al. Management of epilepsy in pregnancy: a report from the International League Against Epilepsy Task Force on Women and Pregnancy. *Epileptic Disord* 2019;21(6):497–517. doi:10.1684/epd.2019.1105
22. Danielsson KC, Borthen I, Morken NH, Gilhus NE. Hypertensive pregnancy complications in women with epilepsy and antiepileptic drugs: a population-based cohort study of first pregnancies in Norway. *BMJ Open* 2018;8(4):e020998. doi:10.1136/bmjopen-2017-020998
23. Prakash C, Hatters-Friedman S, Moller-Olsen C, North A. Maternal and fetal outcomes after lamotrigine use in pregnancy: A retrospective analysis from an urban maternal mental health centre in New Zealand. *Psychopharmacol Bull* 2016;46:63-9.
24. Pennell PB. Use of antiepileptic drugs during pregnancy: Evolving concepts. *Neurotherapeutics* 2016;13:811-20.
25. Li W, Hao N, Xiao Y, Zhou D. Clinical characteristics and pregnancy outcomes of new onset epilepsy during pregnancy. *Medicine (Baltimore)* 2019;98:e16156.
26. Elvedi-Gašparović V, Mikuš M, Beljan P, Živković M, Živković K, Matak L. The impact of antiepileptic treatment in pregnancy on perinatal outcome in Croatia—a single-center study. *ActaClin Croat* 2020; 59:590-6.
27. Jeon JY, Bae JG, Kim KT, Cho YW. Pregnancy and epilepsy: A Korean tertiary epilepsy center review. *Korean Med Sci* 2020;35:e119.
28. Melikova S, Bagirova H, Magalov S. The impact of maternal epilepsy on delivery and neonatal outcomes. *Childs NervSyst* 2020;36:775-82