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# Pregnancy-related Seizure Frequency in Women with Epilepsy: A Single-center Retrospective Study within Current Guidelines

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## Abstract

**Objective:** Epilepsy affects approximately 50 million people worldwide and occurs in 0.5-1% of pregnancies, making seizure management in women with epilepsy (WWE) a major clinical challenge that requires balancing maternal seizure control against fetal safety. This retrospective cohort study evaluated seizure frequency across pregnancy trimesters and the postpartum period in WWE followed at a tertiary referral center and interpreted the findings in light of International League Against Epilepsy guidelines and contemporary evidence.

**Methods:** This retrospective cohort included 49 pregnancies in 47 WWE followed over a four-year period at Ankara Numune Training and Research Hospital and subsequently University of Health Sciences Türkiye, Ankara City Hospitals. In addition to demographic characteristics, seizure type and seizure frequencies before pregnancy, in each trimester (analyzed in three-month intervals), and during the postpartum period were assessed.

**Results:** The mean annual seizure frequency was 0.15±0.31 before pregnancy, 0.08±0.17 during pregnancy, and 0.10±0.26 in the postpartum period, with no significant differences after correction. During pregnancy, seizures decreased in 39.6% of pregnancies, remained stable in 56.25%, and increased in 4.15%. In the postpartum period, seizure frequency decreased in 25.5% of women, remained stable in 57.4%, and increased in 17.0%. Good adherence to medications was significantly associated with lower seizure frequency ($p<0.05$). Epilepsy type, electroencephalography/magnetic resonance imaging abnormalities, and drug serum levels were not significantly associated with changes in seizure frequency.

**Conclusion:** Under structured multidisciplinary care, seizure control during pregnancy in WWE was largely preserved. Adherence to antiseizure medications (ASMs) emerged as the most important modifiable determinant and underscores the critical role of preconception counseling, appropriate ASM selection, and close follow-up during pregnancy and the postpartum period.

**Keywords:** Epilepsy, pregnancy, seizure frequency, antiseizure medications

## INTRODUCTION

Epilepsy is the most common serious neurological disorder requiring continuous pharmacological treatment during pregnancy and affects approximately 50 million people worldwide as well as 0.5-1% of pregnant women.[1,2] The intersection of epilepsy and pregnancy creates a bidirectional chain of risk: pregnancy may alter seizure control through physiological and pharmacokinetic mechanisms, while uncontrolled seizures and the antiseizure medications (ASMs) needed to manage them carry independent risks for maternal and fetal outcomes.[3]

The clinical significance of this intersection is illustrated by data from the European Registry of Antiepileptic Drugs and Pregnancy (EURAP) International Registry, which has prospectively recorded more than 30,594 pregnancies across 47 countries as of November 2024. EURAP data indicate that 58.3% of women with epilepsy (WWE) remain seizure-free during pregnancy, 17.3% experience increased seizure frequency, 15.9% show a decrease, and 63.6% maintain stable seizure patterns compared with the pre-pregnancy period.[4]

WWE represent a clinically vulnerable group in pregnancy because seizure control, maternal safety, teratogenic risk, and neonatal outcomes must be managed simultaneously.[5-8] Both uncontrolled seizures and exposure to certain ASMs can adversely affect pregnancy outcomes, making preconception planning and close monitoring essential.[5,7,9,10]

This single-center retrospective cohort study, conducted over four years at Ankara Numune Research Training and subsequently University of Health Sciences Türkiye, Ankara City Hospitals, provides longitudinal data on seizure frequency dynamics during pregnancy and

the postpartum period. Framed within the 2019/2026 International League Against Epilepsy (ILAE) evidence base and recent large cohort studies, this manuscript aims to offer a clinically applicable synthesis for the management of epilepsy in pregnancy.

## METHODS

### Study Design and Setting

This single-center retrospective cohort study was conducted in the Department of Neurology of Ankara Numune Research Training and later University of Health Sciences Türkiye, Ankara City Hospitals, tertiary academic referral centers, over a four-year study period. The study was designed to characterize the longitudinal trajectory of seizure frequency in WWE before pregnancy, during each pregnancy trimester (in three-month segments), and in the early postpartum period.

### Participants

Consecutive pregnant women with a diagnosis of epilepsy who were followed at the neurology outpatient clinic during the study period were eligible for inclusion. Epilepsy diagnoses were confirmed according to the 2017 ILAE operational classification criteria. The final analysis included 47 women contributing 49 pregnancies. Participants were aged 18-38 years, with the most common age group being 24-34 years. Two women contributed two pregnancies each, while the remaining 45 women contributed one pregnancy. Three pregnancies were excluded from the primary analysis: two early spontaneous miscarriages occurring in the first trimester and one medically terminated pregnancy following detection of a fetal cardiac anomaly after first-trimester valproate (VPA) exposure. This last case is discussed in Section "drug safety profiles and the example of VPA" in the context of VPA teratogenicity.

### Data Collection

Clinical, demographic, and pharmacological data were obtained from electronic medical records and structured epilepsy follow-up notes. Collected variables included epilepsy type (focal, generalized, or unknown onset), etiology, epilepsy duration, ASM regimen (agent, dose, monotherapy versus polytherapy), and seizure type and frequency at each time point (pre-pregnancy, first, second, and third trimesters, and postpartum). Medication adherence was systematically assessed: at each follow-up visit, patients were asked whether they were taking ASMs at the prescribed dose, and this information was recorded. For patients using ASMs with available serum level monitoring, ASM levels were measured and documented, thereby confirming history-based adherence reports. Folic acid use and obstetric outcomes were also recorded for all participants.

**MAIN POINTS**

- Pregnancy has a variable impact on seizure frequency in women with epilepsy, with a substantial proportion remaining stable under appropriate management.
- Adherence to current clinical guidelines, including optimized antiseizure medication regimens and close monitoring, is associated with improved seizure control during pregnancy.
- Changes in seizure frequency are influenced by factors such as baseline seizure control, medication adjustments, and pharmacokinetic alterations during pregnancy.
- A multidisciplinary and individualized approach is essential to minimize maternal and fetal risks while maintaining optimal seizure control.
- Findings from this single-center retrospective study support the importance of guideline-based management in achieving favorable neurological and obstetric outcomes.

### Outcome Definitions

The primary outcome was the change in seizure frequency during pregnancy compared with the pre-pregnancy reference period.

Seizure frequency was categorized as: (a) seizure-free, (b) stable (≤25% change in monthly frequency), (c) decreased (>25% reduction), or (d) increased (>25% increase). Over three-month periods, women with three or fewer seizures were classified as having good seizure control, whereas those with four or more seizures were considered to have poor seizure control. Secondary outcomes included trimester-specific seizure worsening, postpartum seizure course, and the proportion of women requiring ASM dose adjustments.

### Ethical Considerations

The study was conducted in accordance with the Declaration of Helsinki. Institutional review board approval was obtained from the University of Health Sciences Türkiye, Ankara Numune Training and Research Hospital Clinical Research Ethics Committee (approval number: E-18-2317, date: 15.11.2018). Given the retrospective design, the requirement for individual informed consent was waived according to institutional guidelines.

### Statistical Analysis

Longitudinal changes in seizure frequency across time points were analyzed using the Friedman test for non-parametric repeated measures. Pairwise post-hoc comparisons were performed using the Wilcoxon signed-rank test with Bonferroni correction to control the family-wise error rate. Categorical variables were compared using the chi-square test or Fisher's exact test, as appropriate. A two-sided p-value $<0.05$ was considered statistically significant for primary comparisons, and Bonferroni-adjusted thresholds were applied for pairwise tests. All analyses were conducted using SPSS version 26.0 (IBM Corp., Armonk, NY, USA).

## RESULTS

### Baseline Clinical Characteristics

Of the analyzed pregnancies, 53% were first pregnancies and 47% were second or subsequent pregnancies. Maternal age ranged from 18 to 38 years; 34.7% were aged 18-24, 53.1% were 24-34, and 12.2% were ≥35 years. The mean epilepsy duration was 16.66±7.44 years.

Generalized tonic-clonic seizures were present in 59.1% of pregnancies, focal impaired awareness seizures in 32.7%, and focal aware seizures in 8.2% (Figure 1). Etiology was unknown in 71.4% of cases, with infectious, structural, and genetic causes accounting for smaller proportions.

Most pregnancies were managed with monotherapy (45 pregnancies), while only 4 were treated with polytherapy. Common ASMs included levetiracetam (LEV), lamotrigine (LTG), VPA, carbamazepine (CBZ), oxcarbazepine (OXC), topiramate (TPM), and phenytoin (PHT). Specifically, 19 women used LEV, 18 LTG, 7 VPA, 6 CBZ, 1 TPM, 3 OXC, and 1 PHT.

### Seizure Frequency Across Time Periods

Mean seizure frequencies per year were compared across the year before pregnancy, the pregnancy period, and the first postpartum year. In the pre-pregnancy year, the mean seizure frequency among 49 women was 0.15±0.313 (min=0, max=1.66). During pregnancy, the mean frequency among 48 women (one early delivery) was 0.08±0.167 (min=0, max=0.66). In the first postpartum year, the mean seizure frequency was 0.10±0.258 (min=0, max=1.16) in 49 women. Although the Friedman test indicated a statistically significant overall difference over time (with Bonferroni-corrected significance threshold $p<0.016$), none of the pairwise comparisons between periods remained significant in the Wilcoxon signed-rank tests after Bonferroni correction ($p>0.05$). These results are presented in Table 1 and Figure 2.

When analyzed by three-month intervals, mean seizure frequency decreased from 0.11±0.23 in the first trimester to 0.09±0.24 in the second trimester and 0.06±0.16 in the third trimester (Table 2, Figure 3). In postpartum follow-up, the highest mean seizure frequency was observed in the first three months after delivery (0.23±0.56), followed by a gradual decline in subsequent postpartum quarters.

Compared with the pre-pregnancy year, seizure frequency during pregnancy remained unchanged in 56.25% of pregnancies, decreased in 39.6%, and increased in 4.15% (Figure 4). In the comparison between the pre-pregnancy and postpartum periods, seizure frequency decreased in 25.5% of women, remained stable in 57.4%, and increased in 17.0%.

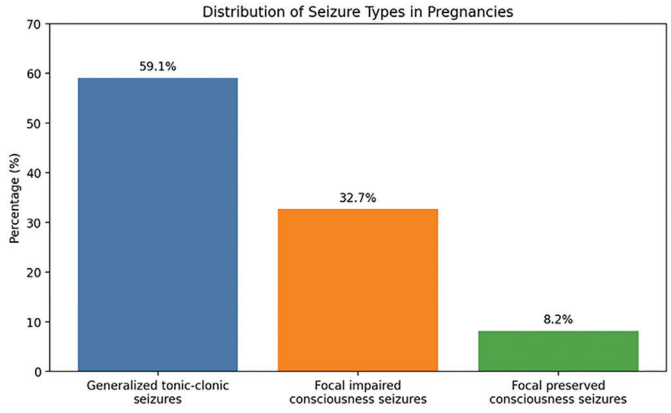


**Figure 1.** Distribution of seizure types among pregnancies

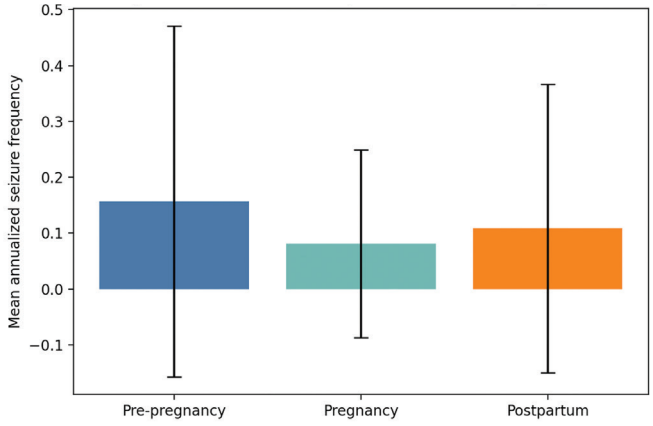


**Figure 2.** Mean seizure frequencies in the year before pregnancy, during pregnancy, and in the first postpartum year

**Table 1.** Seizure frequency expressed as seizures per patient-year and approximate total seizure counts in the pre-pregnancy year, during pregnancy, and in the first postpartum year

| Period | n | Mean seizures (per patient-year) | Median | Minimum (per patient-year) | Maximum (per patient-year) | Approximate total seizures |
|---|---|---|---|---|---|---|
| Pre-pregnancy year | 49 | 0.1571 | 0.0000 | 0.00 | 1.66 | 8 |
| During pregnancy | 48 | 0.0814 | 0.0000 | 0.00 | 0.66 | 4 |
| First postpartum year | 49 | 0.1084 | 0.0000 | 0.00 | 1.16 | 5 |

Overall comparison by Friedman test. Values are presented as number of seizures per patient-year. Minimum and maximum indicate the lowest and highest number of seizures observed in a single patient during the relevant period

**Table 2.** Seizure frequencies by trimester and postpartum quarters

| Period | n | Mean | SD | Median | Minimum | Maximum | Overall p |
|---|---|---|---|---|---|---|---|
| Pre-pregnancy year | 49 | 0.1571 | 0.31389 | 0.0000 | 0.00 | 1.66 | 0.000 |
| 1st trimester | 49 | 0.1147 | 0.22974 | 0.0000 | 0.00 | 1.00 | |
| 2nd trimester | 49 | 0.0878 | 0.24184 | 0.0000 | 0.00 | 1.33 | |
| 3rd trimester | 48 | 0.0600 | 0.16200 | 0.0000 | 0.00 | 1.00 | |
| Postpartum 0-3 months | 49 | 0.2371 | 0.55562 | 0.0000 | 0.00 | 2.66 | |
| Postpartum 3-6 months | 49 | 0.1084 | 0.34164 | 0.0000 | 0.00 | 1.66 | |
| Postpartum 6-9 months | 49 | 0.0608 | 0.22126 | 0.0000 | 0.00 | 1.33 | |
| Postpartum 9-12 months | 49 | 0.0271 | 0.14950 | 0.0000 | 0.00 | 1.00 | |

SD: Standard deviation

### Medication Adherence and Seizure Control

During pregnancy, women who were adherent to their ASM regimen had significantly lower seizure frequency than those who were non-adherent (0.04±0.09 vs. 0.41±0.25, $p<0.05$) (Table 3). Both pre-pregnancy and pregnancy ASM adherence were significantly associated with the distribution of seizure frequency changes between the pre-pregnancy and postpartum periods (Tables 4 and 5). Seizure control according to ASM type is summarized in Figure 5.

### Epilepsy Type, ASM Serum Levels, and Other Tests

The distribution of seizure changes did not differ significantly between generalized and focal epilepsy.

ASM serum levels and their relationship with seizure frequency were assessed separately for each trimester. In the first trimester, among women with subtherapeutic ASM levels, seizure frequency decreased in 20%, remained unchanged in 50%, and increased in 30%; among those with therapeutic levels, seizure frequency decreased in 28.6%, remained unchanged in 61.9%, and increased in 9.5%. In the second trimester, for women with subtherapeutic levels, seizure frequency decreased in 33.3%, remained unchanged in 33.3%, and increased in 33.3%; for those with therapeutic levels, it decreased in 24%, remained unchanged in 64%, and increased in 12%. In the third trimester, among women with subtherapeutic levels, seizure frequency decreased in 40%, remained unchanged in 40%, and increased in 20%; among those with therapeutic levels, it decreased in 23%, remained unchanged in 61.5%, and increased in 15.4%.

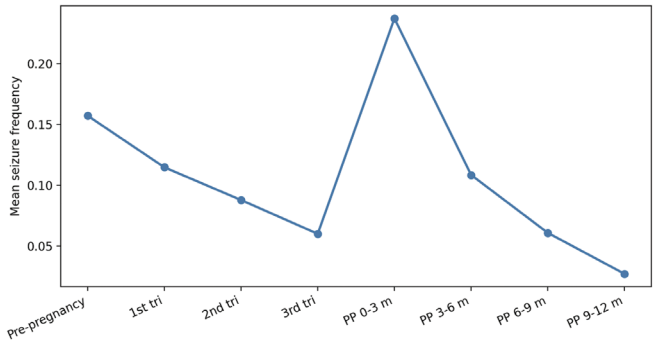


**Figure 3.** Seizure frequency across pre-pregnancy, trimesters, and postpartum quarters

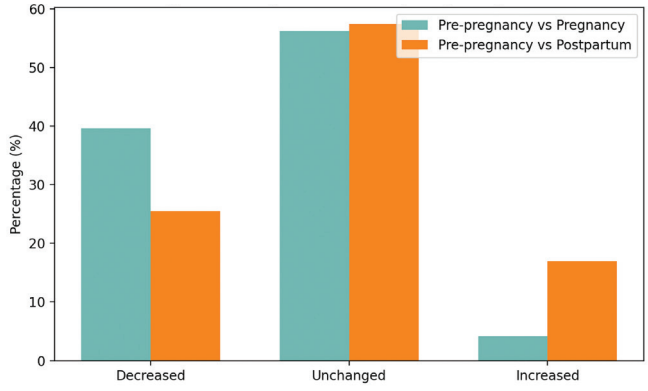


**Figure 4.** Change in seizure frequency from pre-pregnancy to pregnancy and postpartum

**Table 3.** Change in seizure frequency (pre-pregnancy vs. postpartum) according to epilepsy type

| Epilepsy type | Decreased n (%) | Unchanged n (%) | Increased n (%) | Total | p-value |
|---|---|---|---|---|---|
| Generalized | 6 (24.0) | 14 (56.0) | 5 (20.0) | 25 | 0.841 |
| Focal | 6 (27.3) | 13 (59.1) | 3 (13.6) | 22 | |
| Total | 12 (25.5) | 27 (57.4) | 8 (17.0) | 47 | |

**Table 4.** Change in seizure frequency (pre-pregnancy vs. postpartum) according to pre-pregnancy ASM adherence

| Pre-pregnancy ASM adherence | Decreased n (%) | Unchanged n (%) | Increased n (%) | Total | p-value |
|---|---|---|---|---|---|
| Adherent | 6 (16.2) | 26 (70.3) | 5 (13.5) | 37 | 0.002 |
| Non-adherent | 6 (60.0) | 1 (10.0) | 3 (30.0) | 10 | |
| Total | 12 (25.5) | 27 (57.4) | 8 (17.0) | 47 | |

ASM: Antiseizure medication

**Table 5.** Change in seizure frequency (pre-pregnancy vs. postpartum) according to ASM adherence during pregnancy

| ASM adherence during pregnancy | Decreased n (%) | Unchanged n (%) | Increased n (%) | Total | p-value |
|---|---|---|---|---|---|
| Adherent | 9 (21.4) | 27 (64.3) | 6 (14.3) | 42 | 0.023 |
| Non-adherent | 3 (60.0) | 0 (0.0) | 2 (40.0) | 5 | |
| Total | 12 (25.5) | 27 (57.4) | 8 (17.0) | 47 | |

ASM: Antiseizure medication

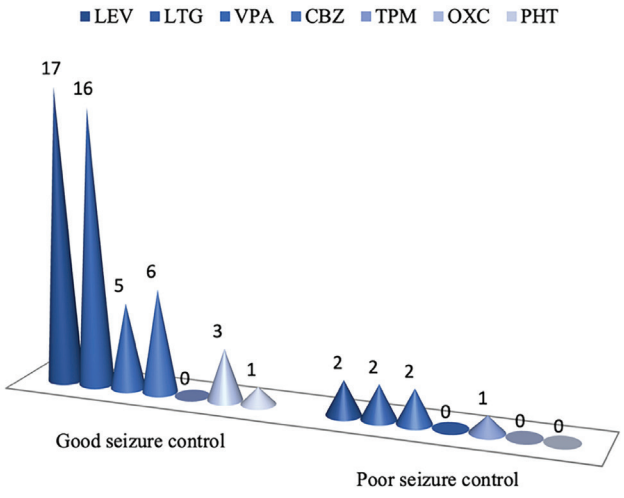


**Figure 5.** Evaluation of seizure control in pregnancy in relation to medication
LEV: Levetiracetam, LTG: Lamotrigine, VPA: Valproate, CBZ: Carbamazepine, OXC: Oxcarbazepine, TPM: Topiramate, PHT: Phenytoin

Across trimesters, no statistically significant association was found between ASM serum level categories and seizure frequency ($p>0.05$).

Similarly, electroencephalography (EEG) and magnetic resonance imaging (MRI) abnormalities were not significantly associated with seizure control during pregnancy.

### Obstetric Outcomes

Two pregnancies ended in spontaneous miscarriage, and one VPA-exposed pregnancy was medically terminated at 24 weeks after prenatal ultrasound detected a fetal cardiac anomaly. The majority of remaining pregnancies resulted in live births, and preterm delivery was rare among women with good seizure control.

## DISCUSSION

### Patterns of Seizure Frequency

The findings from this cohort demonstrate that seizure control remained unchanged in 56.25% of pregnancies, improved in 39.6%, and worsened in only 4.15% compared with the pre-pregnancy year, emphasizing that seizure control is preserved during pregnancy in most women.

Similarly, international evidence strongly supports the fact that the majority of WWEs who did not experience seizures before pregnancy maintained stable seizure control throughout pregnancy. The EURAP International Registry System (n>30,594 pregnancies, 47 countries) reports that 58.3% of WWEs did not experience seizures during pregnancy and 63.6% showed a stable seizure course.[4]

A large prospective multicenter study by Hao et al.,[11] covering 1,110 pregnancies, found that 56.6% of WWEs experienced at least one seizure during pregnancy. In a study by Meador et al.[12] analyzing 1,763 pregnancies, it was reported that approximately two-thirds of pregnancies were stable and 4.4% of offspring had menopausal congenital myelitis (MCM).

Data from Türkiye further confirms this pattern: Korucu et al.[13] found that women who experienced seizures during pregnancy had significantly shorter gestational ages (37.29 vs. 38.24 weeks; $p=0.021$) and lower birth weights (2.587 vs. 3.165 g; $p=0.018$) compared to women who did not experience seizures.

### Epilepsy Type and Syndrome-specific Risk

In our study, the distribution of seizure changes did not differ significantly between generalized and focal epilepsy (Table 5).

When comparing the pre-pregnancy year with pregnancy, seizure frequency remained stable in 56.25% of pregnancies, decreased in 39.6%, and increased in 4.15%; in the comparison between pre-pregnancy and postpartum periods, seizure frequency remained stable in 57.4%, decreased in 25.5%, and increased in 17.0% (Figure 4).

The literature reports an increased risk of seizure worsening during pregnancy in some subtypes of epilepsy. Voinescu et al.[14] showed that focal-onset seizures increased by 21.1% in a cohort of 114 pregnant women during pregnancy, compared to 5.3% for generalized-onset seizures [odds ratio (OR): 4.70; 95% confidence interval (CI): 1.00-22.00; $p=0.050$]. The same study reported that frontal lobe epilepsy carried the highest individual risk (OR: 8.00; 95% CI: 2.19-29.21; $p=0.002$). In contrast, the distribution of seizure changes did not differ significantly between generalized and focal epilepsy in our cohort. This finding may be due to differences in patient characteristics, sample size, or the distribution of epilepsy subtypes.

Similarly, Mostacci et al.[15] showed that 54.5% of pregnancies in women with sleep-related hypermotor epilepsy (SHE) experienced seizure worsening, which is significantly higher than the 17.3% reported in other epilepsy types (OR: 5.7; $p=0.019$; $n=115$). The fact that nocturnal seizures were documented in 34.8% of participants in the current cohort suggests that some of these patients may have an overlap with the SHE phenotype. However, direct assessment of this possibility is not possible due to the lack of detailed classification for SHE diagnosis. Therefore, it would be appropriate to investigate the effect of a history of nocturnal seizures on seizure course during pregnancy in studies with more detailed phenotyping.

### Pharmacokinetic Changes and the Role of Therapeutic Drug Monitoring

Similarly, trimester-based serum ASM level category, EEG abnormality, and MRI abnormality were not found to be statistically significantly associated with seizure control during pregnancy. Pregnancy causes profound physiological changes that systematically reduce plasma concentrations of most ASMs.[3] For LTG, plasma concentrations typically decrease by 40-60%. The MONEAD study[16] found that 74% of participants needed dose adjustment during pregnancy. Schelhaas et al.[17] found that ≥65% reductions in LEV concentration were associated with recurrence of seizures in non-seizure women, and reported that ≥46% reductions were associated with recurrence of seizures in non-seizure women ($p=0.022$).

### Medication Adherence and Patient Education

Our findings show that seizure frequency during pregnancy was significantly lower in women who adhered to their ASM regimens compared with those who did not (Table 4). Both pre-pregnancy and pregnancy adherence were associated with seizure frequency changes across the perinatal period.

The fact that fear of fetal teratogenicity is a reason for non-compliance with medication represents a paradox: the risk of uncontrolled seizures often outweighs the teratogenic risk of most modern antiepileptic drugs.[3] Sevdimbas et al.[18] reported that 41.5% of 53 pregnant epilepsy patients who presented to the emergency department discontinued their medication, and 47% of those who discontinued their medication required hospitalization ($p<0.001$).

### Drug Safety Profiles and the Example of VPA

In this cohort, one of seven VPA-exposed pregnancies was medically terminated because of a fetal cardiac anomaly, a finding consistent with the broader literature on VPA-associated teratogenicity. However, this case represents an individual clinical course rather than a systematically analyzed variable within the study. Previous extensive evidence has shown that VPA exposure is associated with a dose-dependent increase in major congenital malformations and adverse neurodevelopmental outcomes; therefore, both guidelines and regulatory bodies do not recommend its use in women of childbearing age when safer alternatives are available.[7,10,19,20]

VPA remains the most significant pharmacological safety concern in pregnancies in women of reproductive age. A cochrane review by Bromley et al.[21] and independent meta-analyses confirm an approximate MCM rate of 9.8% (95% CI: 8.1-11.9) in pregnancies exposed to VPA Bjørk et al.[22] identified risks of autism spectrum disorder (OR: 2.98; 95% CI: 2.23-3.99) and intellectual disability (OR: 2.48; 95% CI: 1.71-3.59).

Turkish data confirm these international findings. In Türkiye's most comprehensive multicenter prospective study, involving 759 pregnant WWE women in 21 centers, Pekoz et al.[23] found that VPA showed the highest incidence of MCM (8.5%), while LTG had the lowest (2.1%). Kalaycı Yiğin et al.[24] reviewed teratology counseling data for 10,562 pregnancies and reported a statistically significantly higher prevalence of major and minor anomalies and behavioral disorders in children of women using VPA.

### Monotherapy Versus Polytherapy

Most pregnancies were managed with monotherapy (45 pregnancies), while only 4 pregnancies were followed under polytherapy. Commonly used antiepileptic drugs included LEV, LTG, VPA, CBZ, OXC, TPM, and PHT. A comparison in terms of seizure control is summarized in Figure 5.

The predominance of monotherapy (91%) in the current cohort reflects robust clinical practice. In EURAP records, polytherapy was associated with an OR of 9.0 (95% CI: 5.6-14.8) for seizure occurrence compared to monotherapy.[4] Voinescu et al.[14] found that polytherapy provided an OR of 8.36 (95% CI: 2.07-33.84; $p=0.003$) for seizure worsening.

Pekoz et al.[23] found that the risk of MCM in the children of women receiving polytherapy was 2.31 times higher (13.7% vs. 5.7%). Demiral et al.[25] showed that the rates of gestational diabetes and congenital malformations were significantly higher in the polytherapy group. Gul et al.[26] found that the number of ASMs used in multivariate logistic regression was an independent predictor of adverse outcomes.

### Study Limitations

This study has several limitations related to its retrospective, single-center design. Referral bias to a tertiary center may limit generalizability to community settings. Because 47 women contributed 49 pregnancies, with two women having two pregnancies each, the assumption of independence between observations is partially limited. Furthermore, reviewing data such as the effect of postpartum seizure increase on patients, the presence of possible accompanying sleep disturbances, medication adherence, and patients' individual teratogenicity concerns could enrich the study. Although the patients participating in the study were randomly selected based on their referral, the fact that they were patients with relatively infrequent seizures means that the data may not fully contribute to pregnancy management in all epileptic patients, including those with refractory cases. Despite these limitations, the findings demonstrate internal consistency and agreement with international evidence. This study, along with contributions from Pekoz et al.,[23] Gul et al.,[26] Korucu et al.,[13] Demiral et al.[25] and others, contributes to the growing Turkish epilepsy-pregnancy literature.

## CONCLUSION

This retrospective cohort study of 49 pregnancies in WWE followed at Ankara Numune Training and Research Hospital and subsequently University of Health Sciences Türkiye, Ankara City Hospital confirms that pre-pregnancy seizure status is the key determinant of seizure frequency during pregnancy. In most women whose epilepsy was effectively controlled before conception, seizure control remained stable throughout pregnancy.

### Ethics

**Ethics Committee Approval:** Institutional review board approval was obtained from the University of Health Sciences Türkiye, Ankara Numune Training and Research Hospital Clinical Research Ethics Committee (approval number: E-18-2317, date: 15.11.2018).

**Informed Consent:** Given the retrospective design, the requirement for individual informed consent was waived according to institutional guidelines.

### Footnotes

### Authorship Contributions

Surgical and Medical Practices: B.K., A.P.T., Concept: A.P.T., Design: A.P.T., Data Collection or Processing: B.K., A.P.T., Analysis or Interpretation: B.K., A.P.T., Literature Search: B.K., A.P.T., Writing: B.K., A.P.T.

**Conflict of Interest:** No conflict of interest was declared by the authors.

**Financial Disclosure:** The authors declared that this study received no financial support.

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