Van Med J 32 (3):195 -203, 2025
DOI: 10.5505/vmj.2025.64426

Obstetric and Perinatal Outcomes in Pregnant Women with Epilepsy: A Comparative Study of Monotherapy and Polytherapy

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Abstract

Introduction: This study aimed to evaluate the clinical, obstetric, and perinatal outcomes of pregnant women with epilepsy and to investigate the impact of antiepileptic drug (AED) regimens (monotherapy versus polytherapy) on these outcomes.

Materials and Methods: This retrospective study included 98 singleton pregnancies with epilepsy who delivered at a tertiary referral center between October 2022 and May 2025. Patients were grouped based on AED use: monotherapy or polytherapy. Composite adverse perinatal outcome (CAPO), including preterm birth, NICU admission, low Apgar scores, and neonatal complications, was the primary outcome. Univariate and multivariate logistic regression analyses were performed to identify factors associated with CAPO.

Results: Among the participants, 76 (77.6%) received antiepileptic treatment; 60 (61.2%) received monotherapy and 16 (16.3%) received polytherapy. CAPO occurred in 37.8% of all cases, with a significantly higher rate in the polytherapy group compared to the monotherapy group. Seizure during pregnancy, cesarean delivery due to fetal distress, and lower birth weight were more frequent in the polytherapy group. In multivariate analysis, polytherapy was identified as an independent predictor of CAPO (aOR: 10.609; 95% CI: 1.617-69.604), while higher gestational age at delivery was protective.

Conclusion: This study revealed that cases of polytherapy resulted in significantly elevated incidence of seizures during pregnancy, cesarean sections due to fetal distress, low birth weight, and CAPO compared to monotherapy. The data suggest that the use of multiple antiepileptic drugs may adversely affect perinatal outcomes by increasing fetal exposure.

Key words: Epilepsy; pregnancy; anticonvulsants; pregnancy complications; perinatal outcome; polypharmacy

Introduction

Epilepsy is a chronic neurological disorder characterized by recurrent, spontaneous seizures caused by abnormal electrical activity in the brain (1). It affects approximately 1% of women of reproductive age (2). Pregnant women with epilepsy present a unique clinical challenge requiring careful balance between effective seizure control and minimizing potential risks to both the mother and fetus. Although the overall prevalence of epilepsy in pregnancy is comparable to that in the general population, the physiological and hormonal changes associated with pregnancy can significantly alter seizure patterns and treatment responses (3). Studies show that epilepsy affects between 0.5% and 1% of pregnant women, and its presence demands individualized care strategies. Managing epilepsy during this period involves navigating the dual concerns of maternal safety and fetal well-being (4). Pregnant women with epilepsy are at an increased risk for complications such as preeclampsia, gestational diabetes, and preterm birth (5,6). In addition, some antiepileptic drugs (AEDs) are known to carry teratogenic potential, heightening concerns about congenital anomalies in newborns (7-10). Moreover, pregnancy can affect the pharmacokinetics of AEDs, leading to fluctuations in drug levels that may increase or decrease seizure frequency. For this reason, continuous monitoring and timely adjustments in treatment are essential to optimize outcomes for both mother and child. Antiepileptic drugs (AEDs) are known to be an independent risk factor for adverse neonatal outcomes (8,9). Some AEDs-particularly valproic acid and topiramate-ve been linked to complications such as fetal growth restriction, preterm birth, low birth weight, congenital anomalies, neurodevelopmental delays, and even autism spectrum(8). While newer-generation medications like lamotrigine and levetiracetam appear to carry a lower teratogenic

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Received: 07.05.2025, Accepted: 23.06.2025

risk, treatment during pregnancy still requires a careful balance between effective seizure control and fetal safety (8). Current evidence supports that monotherapy is generally associated with better neonatal outcomes and a reduced risk of congenital malformations compared to polytherapy (8). For this reason, pre-pregnancy counseling, thoughtful selection of antiepileptic agents, timely dose adjustments, and close multidisciplinary follow-up throughout pregnancy are essential components of care. However, managing epilepsy becomes more challenging in unplanned pregnancies or in those with limited prenatal monitoring, where these preventive strategies may not be optimally applied. The main objective of this study is to evaluate the clinical, obstetric, and neonatal outcomes of pregnant women diagnosed with epilepsy at a tertiary referral center. In addition, the impact of the antiepileptic treatment regimen (monotherapy versus polytherapy) on pregnancy outcomes will be investigated.

Materials and Methods

Study design and setting: This retrospective, descriptive study aims to evaluate the clinical and obstetric characteristics of pregnant women with epilepsy who gave birth between October 2022 and May 2025 in the Ankara Etlik City Hospital. The research was performed in compliance with the Declaration of Helsinki and obtained approval from the local ethics committee (Ethics Committee Approval Number: AEŞH-BADEK2-2025-003). Informed consent was waived because the study was retrospective in nature.

Participants: The study cohort comprised all singleton pregnancies of women with epilepsy who delivered between October 2022 and May 2025. Patients with systemic or neurological conditions other than epilepsy, those who received postnatal care or delivered at another institution, those with incomplete clinical data, multiple gestations, maternal chronic diseases unrelated to epilepsy, or fetuses with structural or chromosomal anomalies were excluded from the study. In addition, pregnant women with epilepsy who participated in the study and received AED treatment were divided into two subgroups based on the number of antiepileptic drugs administered: Monotherapy (one drug) and polytherapy (more than one drug). Cases that developed status epilepticus throughout pregnancy, follow-up, and delivery were excluded from the research.

Variables and data sources: This study examines demographic, obstetric, epilepsy-related, and perinatal characteristics of the patients. All data were retrospectively reviewed using the hospital's electronic record system and recorded on a standardized data collection form. Demographic characteristics included maternal age, maternal body mass index (BMI), gravidity, and number of parities. Variables related to epilepsy included duration of epilepsy (in years), interval since last seizure (in months), occurrence of seizures during pregnancy, frequency of seizures in cases where seizures occurred during pregnancy, trimester in which these seizures occurred, use of antiepileptic drug (AED) treatment, treatment regimen (monotherapy or polytherapy), and the active ingredient of the AED administered. Obstetric data include the type of delivery (spontaneous vaginal delivery, cesarean section) and the occurrence of adverse events during pregnancy (e.g. gestational hypertension, gestational diabetes, fetal growth restriction, pre-eclampsia, placental abruption, postpartum hemorrhage). Neonatal outcomes include gestational age, birth weight, occurrence of fetal distress, a 5-minute APGAR score of 7 or lower, preterm birth, admission to the neonatal intensive care unit (NICU), occurrence of neonatal sepsis, occurrence of neonatal hypoglycemia, and respiratory distress syndrome. Composite adverse perinatal outcome (CAPO) was defined as the occurrence of any of the following: fetal distress, a 5-minute APGAR score of ≤7, admission to the NICU, neonatal sepsis, neonatal hypoglycemia, respiratory distress syndrome, or preterm birth. Cases with incomplete clinical or outcome data were not included in the study.

Statistical analysis: All statistical analyses were conducted utilizing SPSS Statistics 27.0 software (IBM Corp., Armonk, NY, USA). The normal distribution was evaluated with the Kolmogorov-Smirnov and Shapiro-Wilk tests. Continuous variables exhibiting normal distribution were represented as mean ± standard deviation (SD), while those without normal distribution were represented as median (25th – 75th percentile). Categorical variables were represented as counts and percentages (n, %). Subgroup analyses were conducted between the monotherapy and polytherapy cohorts. Student's t-test was employed for continuous variables with normal distribution, while the Mann-Whitney U-test was utilized for those with non-normal distribution. The chi-square test or Fisher's exact test was utilized when suitable for comparing categorical variables. Univariate and multivariate logistic regression analyses were performed to determine the factors predicting the development of a composite unfavorable perinatal outcome (CAPO) in treated epilepsy patients (n=80). In the univariate analyses, variables hypothesized to be

Table 1: Demographic and clinical characteristics of pregnant women with epilepsy

Pregnant women with epilepsy (n)	98
Age (years), median (25-75 percentile)	28 (24-33)
Gravidity, median (25-75 percentile)	2 (1-3)
Parity, median (25-75 percentile)	1 (0-1)
BMI (kg/m²), mean ± SD	29.36 ± 5.69
Smoking, n(%)	15 (15.3%)
Time since epilepsy diagnosis (years), median (25-75 percentile)	8.0 (6.0-15.0)
Treatment	
No Treatment, n(%)	22 (22.4%)
Active Treatment, n(%)	76 (77.6%)
Monotherapy, n(%)	60 (61.2%)
Polytherapy , n(%)	16 (16.3%)
Seizure During Pregnancy	
No, n(%)	61 (62.2%)
Yes, n(%)	37 (37.8%)
Number of Seizures During Pregnancy, median (25-75 percentile)	0 (0-1)
Trimester of Seizure Occurrence	
1st Trimester, n(%)	13 (35.1%)
2nd Trimester, n(%)	15 (40.5%)
3rd Trimester, n(%)	24 (64.9%)

Note: Since some patients experienced seizures in more than one trimester, the percentages exceed 100%.
Abbreviations: SD, Standard deviation; BMI, Body mass index.

Table 2: Distribution of antiepileptic drug use in pregnant women with epilepsy

Antiepileptic Drug	Total Use (n=76)		Monotherapy (n=60)		Polytherapy (n=16)	
	n, (%)	Mean dose (minimum-maximum)	n, (%)	Mean dose (minimum-maximum)	n, (%)	Mean dose (minimum-maximum)
Levetiracetam	54 (71.1%)	1373 (500-3000)	39 (65.0%)	1295 (500-3000)	15 (93.8%)[1]	1567 (1000-3000)
Lamotrigine	17 (22.4%)	139 (50-300)	14 (23.3%)	146 (50-300)	3 (18.8%)[2]	125 (50-200)
Carbamazepine	18 (23.7%)	475 (200-800)	5 (8.3%)	300 (200-400)	13 (81.3%)[3]	545 (400-800)
Valproate	3 (3.9%)	667 (250-1500)	2 (3.3%)	250 (250-250)	1 (6.2%)[4]	1500 (1500-1500)

[1] Includes 12 cases combined with carbamazepine, and 3 cases combined with lamotrigine
[2] All in combination with levetiracetam
[3] Includes 12 cases combined with levetiracetam, and 1 with valproate
[4] Combined with carbamazepine in one case
Note: Drug doses are presented as mean (minimum–maximum) in milligrams (mg).

associated with CAPO were included separately in the model. Variables that were found to be significant ($p < 0.05$) and clinically meaningful were analyzed together in the multivariate analysis. In the multivariate logistic regression analysis, all variables were included in the model simultaneously (the enter method was used), and the results were reported with odds ratio (OR), 95% confidence interval (CI), and p-value. Missing data were checked before analysis, and cases with missing records were not included in the study. In all analyses, the level of statistical significance was accepted as $p < 0.05$.

Results

Data were collected from 120 pregnant women with epilepsy who were monitored and delivered in our hospital. Of these cases, cases six were excluded due to incomplete clinical or outcome data, three were excluded because of chronic hypertension, one because of type 1 diabetes mellitus, two because of type 2 diabetes mellitus, one because of systemic lupus erythematosus (SLE), five cases were excluded from the study due to the development of status epilepticus, and four because of twin pregnancies; thus, 98 pregnant women with epilepsy were included in the study. The demographic and clinical characteristics of the pregnant women with epilepsy included in the study are shown in Table 1. The median age of the participants was 28 years, the median gravida number was 2, and the number of parities was 1. The mean BMI was 29.36 ± 5.69 kg/m². 15.3% of the participants were identified as smokers. The median period from the diagnosis of epilepsy was 8.0 years (range: 6.0–15.0 years). 77.6% of patients were on antiepileptic treatment, of which 61.2% were on

monotherapy and 16.3% on polytherapy. During the entire pregnancy period, 37.8% of the patients experienced at least one seizure, with 64.9% of these seizures occurring in the third trimester. Table 2 shows the treatment regimens and corresponding dosages of the 76 pregnant women who were treated for epilepsy with antiepileptic drugs. The most commonly used drugs were levetiracetam (71.1%; mean dose, 1373 mg; range, 500–3000 mg), followed by lamotrigine (22.4%; mean dose, 139 mg; range, 50–300 mg), carbamazepine (23.7%, mean dose, 475 mg; range, 200–800 mg), and valproate (3.9%; mean dose, 667 mg; range, 250–1500 mg). In the polytherapy cohort, 93.8% of patients included levetiracetam in their treatment regimen, often in combination with carbamazepine (81.3%) or lamotrigine (18.8%). In the Monotherapy group, levetiracetam was the most frequently used drug, accounting for 65.0% of cases, followed by lamotrigine (23.3%), carbamazepine (8.3%), and valproate (3.3%).When the obstetric and perinatal outcomes of pregnant women with epilepsy were analysed (Table 3), the main obstetric problems identified were gestational diabetes (13.3%) and fetal growth restriction (9.2%).

Table 3: Obstetric and perinatal outcomes of pregnant women with epilepsy

Obstetric Outcomes	
Gestational Hypertension, n(%)	3 (3.1%)
Preeclampsia, n(%)	1 (1.0%)
Gestational Diabetes Mellitus, n(%)	13 (13.3%)
Fetal Growth Restriction, n(%)	9 (9.2%)
Placental Abruption, n(%)	2 (2.0%)
Postpartum Hemorrhage, n(%)	1 (1.0%)
Gestational Age at Delivery, median (25-75 percentile)	38 (37-39)
Birth Weight, mean ± SD	2949 ± 702
Mode of Delivery	
Vaginal, n(%)	24 (24.5%)
Cesarean Section, n(%)	74 (75.5%)
Perinatal Outcomes	
Premature Rupture of Membranes, n(%)	10 (10.2%)
Cesarean Section Due to Fetal Distress, n(%)	13 (13.3%)
Preterm Birth, n(%)	21 (21.4%)
5-minute Apgar Score ≤7, n(%)	9 (9.2%)
Respiratory Distress Syndrome, n(%)	12 (12.2%)
NICU admission, n(%)	17 (17.3%)
Neonatal Sepsis, n(%)	1 (1.0%)
Neonatal Hypoglycemia, n(%)	3 (3.1%)
CAPO, n(%)	37 (37.8%)

Abbreviations: SD, Standard deviation; NICU, Neonatal intensive care unit; CAPO, Composite adverse perinatal outcome.

The preterm birth rate was 21.4%, while the cesarean section rate was 75.5%. The mean birth weight at neonatal outcome assessment was 2949 ± 702 grams. The NICU admission rate was 17.3%, the 5-minute Apgar score of ≤7 was 9.2%, and the RDS rate was 12.2%. A composite adverse perinatal outcome (CAPO) was found in 37 individuals, corresponding to 37.8%.

Table 4: Comparison of clinical, obstetric, and perinatal characteristics between monotherapy and polytherapy groups in pregnant women with epilepsy

Variables	Monotherapy (n=60)	Polytherapy (n=16)	p-value
Age (year)	27 (24-33)	32 (28-33)	0.061[a]
Gravidity	2 (1-3)	2 (1-3)	0.784[a]
Parity	1 (0-1)	1 (0-2)	0.826[a]
BMI (kg/m²)	29.43 ± 5.50	28.65 ± 8.49	0.654[b]
Seizure During Pregnancy	23 (38.3%)	11 (68.8%)	**0.030[c]**
Obstetric Outcomes			
Gestational Hypertension	2 (3.3%)	1 (6.3%)	0.513[d]
Preeclampsia	1 (1.7%)	-	N/A
Gestational Diabetes Mellitus	7 (11.7%)	3 (18.8%)	0.431[d]
Fetal Growth Restriction	4 (6.7%)	2 (12.5%)	0.600[d]
Placental Abruption	2 (3.3%)	-	N/A
Postpartum Hemorrhage	1 (1.7%)	-	N/A
Gestational Age at Delivery (weeks)	38 (37-39)	38 (35-39)	0.711[a]
Birth Weight (gr)	3041 ± 685	2605 ± 676	**0.032[b]**
Perinatal Outcomes			
Preterm Birth	12 (20.0%)	5 (31.3%)	0.333[d]
PROM	4 (6.7%)	2 (12.5%)	0.600[d]
Cesarean Section Due to Fetal Distress	6 (10.0%)	5 (31.3%)	**0.047[d]**
5-minute Apgar Score ≤7	6 (10.0%)	3 (18.8%)	0.387[d]
Respiratory Distress Syndrome	6 (10.0%)	3 (18.8%)	0.387[d]
NICU Admission	7 (11.7%)	5 (31.3%)	0.115[d]
Neonatal Sepsis	1 (1.7%)	-	N/A
Neonatal Hypoglycemia	1 (1.7%)	1 (6.3%)	0.379[d]
CAPO	18 (30.0%)	10 (62.5%)	**0.017[c]**

[a] Mann–Whitney U test was used; data are presented as median (25th–75th percentile).
[b] Independent samples t-test was used; data are presented as mean ± standard deviation.
[c] Chi-square test was used; data are presented as number (%).
[d] Fisher's exact test was used; data are presented as number (%).
Abbreviations: BMI, Body Mass Index; N/A, Not applicable; PROM, Premature Rupture of Membranes; NICU, Neonatal Intensive Care Unit; CAPO, Composite Adverse Perinatal Outcome.

Table 5. Factors associated with composite adverse perinatal outcome (CAPO) among epileptic pregnant women receiving antiepileptic treatment: results of univariate and multivariate logistic regression analyses

Variables	Univariate			Multivariate		
	OR	95% CI	p-value	aOR	95% CI	p-value
Monotherapy vs. Polytherapy	3.889	1.228-12.318	0.021	10.609	1.617-69.604	0.014
Duration of Epilepsy (year)	0.974	0.907-1.045	0.461	0.946	0.846-1.057	0.326
Seizure Occurrence During Pregnancy	1.400	0.548-3.573	0.482	0.579	0.052-6.496	0.658
Number of Seizures During Pregnancy	0.989	0.680-1.437	0.952	0.740	0.279-1.964	0.546
Gestational Age at Delivery	0.461	0.302-0.703	0.001	0.446	0.258-0.773	0.004
Birth Weight	0.998	0.997-0.999	0.001	1.000	0.998-1.001	0.509

Abbreviations: OR, Odds ratio; CI, Confidence interval; aOR, Adjusted odds ratio.

Table 4 shows a comparison of the obstetric and perinatal outcomes between the monotherapy and polytherapy groups. The incidence of seizures was significantly increased in pregnant patients receiving polytherapy compared to those receiving monotherapy (68.8% vs. 38.3%, p = 0.030). The polytherapy group had a significantly lower birth weight (p=0.032), although no significant difference was found in gestational age at delivery (p=0.711). The rate of cesarean deliveries due to fetal distress was significantly higher in the polytherapy group (p=0.047). The CAPO rate was 62.5% in the polytherapy group and 30.0% in the monotherapy group (p = 0.017). Table 5 shows univariate and multivariate logistic regression analyses to assess characteristics associated with CAPO. In the univariate analysis, polytherapy (p = 0.021), low gestational age at delivery (p =

0.001), and low birth weight (p = 0.001) were found to be significant risk factors for CAPO. In the multivariate analysis, only polytherapy (aOR: 10.609; 95% CI: 1.61-69.60; p = 0.014) and gestational week at birth (aOR: 0.446; CI: 0.25-0.77; p = 0.004) were independently associated with CAPO. In the multivariable model, the duration of epilepsy (aOR: 0.946, p=0.326), the occurrence of seizures during pregnancy (aOR: 0.579, p=0.658), the number of seizures (aOR: 0.740, p=0.546), and birth weight (aOR: 1.000, p=0.509) showed no significant correlation with CAPO.

Discussion

This study examined the obstetric and neonatal outcomes of pregnant women with epilepsy. The cesarean section rate in pregnant women with epilepsy was 75.5%, with the predominant obstetric problems being gestational diabetes mellitus (13.3%) and fetal growth restriction (9.2%). In addition, our study examined individuals undergoing monotherapy and polytherapy to assess the impact of the different treatment regimens on pregnancy outcomes. In addition, the incidence of seizures, cesarean delivery due to fetal distress, and CAPO was significantly increased in the polytherapy cohort. The logistic regression analysis showed that polytherapy and low gestational age were independent predictors of CAPO. The choice of pharmacologic treatment for epilepsy in pregnant women has a significant impact on obstetric and neonatal outcomes. Monotherapy, in which a single antiepileptic drug is administered, is associated with lower teratogenic, obstetric, and neonatal risks. In contrast, polytherapy, the simultaneous use of several drugs, is preferred for resistant epilepsy, but carries increased fetal and neonatal risks. In the study by Çim et al., 26.3 % of pregnant women with epilepsy were not receiving any active treatment, 78.9 % were receiving monotherapy, and 18 % were receiving polytherapy (11). In another study, Richmond et al. reported that 16.5% of patients were not receiving active treatment, 64.3% were receiving monotherapy, and 19.2% were receiving polytherapy (12). In our study, 22.4% of patients were not on active treatment, 61.2% received monotherapy, and 16.3% received polytherapy. In this respect, our work is congruent with the existing literature. In pregnant women with epilepsy, the occurrence of seizures and status epilepticus during pregnancy is a critical factors that directly influence both maternal and fetal outcomes. Barroso et al. showed that 60% of patients experienced at least one seizure during pregnancy (13). Thomas et al. pointed out that 47% of pregnant women with epilepsy were seizure-free during their pregnancy; nevertheless, status epilepticus occurred in three cases (14). In the study conducted by Gül et al., the frequency of seizures was 39.1%(15). Our study found that 62.2% of pregnant women with epilepsy remained seizure-free during their pregnancy, while 37.8% experienced seizures. The data suggest that the frequency of seizures in our study is consistent with some studies in the literature. Inadequate treatment of seizures increases the likelihood of problems in the mother and correlates with adverse effects on the newborn, including fetal distress, preterm delivery, and reduced Apgar scores. Therefore, it is crucial to carefully monitor pregnant women with epilepsy from both a neurological and obstetric perspective through a multidisciplinary approach. The challenges of managing seizures in pregnant women with epilepsy, fetal exposure to antiepileptic medications, and pregnancy-related physiologic changes increase the risk of obstetric and neonatal problems, including preterm labor, preeclampsia, and fetal distress (13,14). The study by Çim et al. in pregnant women with epilepsy documented the incidence of preterm labor at 18.4%, preeclampsia at 5.3%, and fetal distress at 2.6%; it also highlighted that an increase in seizure frequency during pregnancy correlates with a decreased 5-minute Apgar score (11). Our study found a preterm birth rate of 21.4%, a cesarean section rate due to fetal distress of 13.3%, and a 5-minute Apgar score of ≤7 in 9.2% of cases. Although these rates are broadly comparable to the statistics presented by Çim and colleagues, they are elevated in some respects. This fact may be attributed to the clinical characteristics of the patient cohort, differences in treatment efficacy, or disparities in the provision of healthcare services. The occurrence of seizures and the physiological stress associated with epilepsy may have a negative impact on the fetus, suggesting that pregnant women with epilepsy are at increased risk throughout the perinatal period and need to be monitored vigilantly. Our study found that when evaluating the impact of antiepileptic treatment regimens on pregnant women with epilepsy on obstetric and perinatal outcomes, there was a higher level of adverse pregnancy outcomes in the polytherapy group. During pregnancy, the incidence of seizures was significantly higher in the polytherapy group (68.8% vs. 38.3%, p=0.030). These data are broadly consistent with the studies by Prameeda et al., who found a seizure rate of 48% in the monotherapy group and 33.3% in the polytherapy group, although this

difference was not statistically significant (16). The cesarean section rate due to fetal distress was significantly increased in the polytherapy group in our study (31.3% vs. 10.0%, p=0.047); however, Prameeda et al. found no significant difference between the groups in terms of fetal distress and meconium-containing amniotic fluid (16). Our study found that birth weight was significantly lower in the polytherapy group, whereas Prameeda and colleagues found no significant difference in this aspect (16). The most notable finding of our study is the significantly increased composite adverse perinatal outcome (CAPO) rate in the polytherapy group (62.5% vs. 30.0%, p=0.017). This finding suggests that exposure to multiple antiepileptic drugs may increase prenatal risks, which emphasizes its importance given the sparse evidence in the literature on this topic(8,17). Our research shows that pregnant women with epilepsy who require polytherapy have an increased risk of perinatal problems, justifying closer monitoring of this patient group during pregnancy. Moreover, although major congenital malformations (MCMs) were not included as predefined outcome parameters in our investigation, it is crucial to recognize that dose-dependent teratogenic risks associated with specific antiepileptic drugs (AEDs) are well-documented in the literature(8,18–21). Prior research has repeatedly shown that high doses of valproate and carbamazepine correlate with a heightened risk of MCMs (8,18,19). No definitive dose-response relationship for lamotrigine concerning MCM risk has been established; yet, a weak correlation with neurodevelopmental disorders (NDDs) has been reported (20). No dose-dependent teratogenic effects of levetiracetam have been demonstrated in monotherapy; nevertheless, an elevated risk of NDDs has been observed in certain polytherapy combinations, such as levetiracetam combined with carbamazepine(20). In our investigation, the limited sample size of the polytherapy group (n = 16) and the exclusion of individuals with fetal structural or chromosomal anomalies precluded a direct assessment of the dose-dependent effects of AEDs. Nonetheless, the markedly elevated CAPO rate observed in the polytherapy cohort may partly reflect greater cumulative AED exposure within this group. Future large-scale prospective studies are needed to further elucidate the dose-dependent effects of different antiepileptic medications and their combinations on maternal and neonatal outcomes. In the logistic regression analysis performed to investigate the determinants of CAPO in pregnant women with epilepsy, we discovered that early gestational weeks at delivery and polytherapy regimens were strongly linked with CAPO. In the univariate analysis, the probability of developing CAPO in the polytherapy group was 3.88 times greater, whereas in the multivariate analysis, it was 10.60 times greater. Furthermore, our findings indicate that each weekly increment in gestational age at birth reduces the likelihood of developing CAPO by approximately 45% (aOR: 0.446, p = 0.002). Conversely, in the multivariate analysis, the duration of epilepsy and the existence and frequency of seizures during pregnancy were not correlated with CAPO. The data indicate that the polytherapy regimen in the treatment protocol may negatively impact perinatal outcomes. Consistent with our findings, research by Thomas et al. and Barroso et al. has indicated that unfavorable perinatal complications are more prevalent, especially among patients with low birth weight and those using polytherapy (13,14).

Study limitations: Our research possesses certain limitations. The primary aspect is that the study is retrospective. Furthermore, the restricted data regarding the types of seizures occurring during pregnancy precluded an assessment of the influence of seizure type on pregnancy and neonatal outcomes. The study's execution in a single center constrains the generalizability of the findings. Due to the inability to document crucial pharmacokinetic data, such as serum concentrations of antiepileptic medicines and treatment adherence, one must use caution when interpreting specific results related to drug effects. The restricted size of the study population may have hindered the attainment of statistical significance in specific subgroups.

Conclusion

In conclusion, this study demonstrates that antiepileptic medication regimen administered to pregnant women with epilepsy can significantly affect obstetric and perinatal outcomes. Patients receiving polytherapy were more likely to experience seizures, fetal distress, low birth weight, and composite adverse perinatal outcomes (CAPO) during pregnancy. In multivariable analyses, polytherapy and early gestational age at birth were found to be independent risk factors for the occurrence of CAPO. These findings suggest that pregnant women with epilepsy need to be monitored by personalized treatment strategies and, if possible, should be guided to monotherapy. In addition, careful obstetric monitoring and a multidisciplinary approach are essential to improve maternal and fetal outcomes in this patient group. Future large, prospective, and multicenter studies will improve the treatment

of pregnant women with epilepsy by expanding the applicability of the data obtained.

Acknowledgement: None
Conflict of interest: The authors have no conflict of interest regarding this study.
Ethical approval: Ethics Committee permission (without specifying the institution from which it was obtained) was obtained from Ankara Etlik City Hospital Clinical Research Ethics Committee with the decision number: AEŞH-BADEK2-2025-003
Statement of financial support: No financial support has been received for this study.
Author Contributions: Concept (R.T.A., Ö.V.A.), Design (R.T.A., Ö.V.A., K.Ç.), Data Collection (Ö.V.A., B.A., G.K.), Data Processing (K.Ç., G.K.), Analysis (R.T.A., A.A.F.,), Literature Review (R.T.A., A.K., A.Ç.B.), Materials (A.A.F., B.A.), Writing – Original Draft (R.T.A.), Writing – Review and Revision (R.T.A., A.Ç.B., Z.V.Y.), Critical Review (Z.V.Y.), Audit (A.K., K.Ç.).
Data sharing statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

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