



ORIGINAL ARTICLE

Epilepsy and Pregnancy: Retrospective Analysis of 58 Cases

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Abstract

Introduction: This study aimed to retrospectively evaluate the perinatal outcomes of pregnant women diagnosed with epilepsy followed in our clinic.

Methods: In this retrospective cohort study, a total of 58 pregnant women diagnosed with epilepsy who were delivered after pregnancy follow-up at Sakarya University Training and Research Hospital Gynecology and Obstetrics Clinic between January 2015 and March 2021 were evaluated.

Results: The mean age of the patients was 28.4±5.7 years. It was determined that 25 cases (43.1%) had seizures during pregnancy. It was determined that the rate of seizures during pregnancy in those who had a seizure in the past 1 year before pregnancy was statistically significantly higher than those who had their last seizure longer than 1 year (p=0.000). It was found that 72.7% of the patients in the polytherapy group had epileptic seizures during pregnancy, and this rate was significantly higher than the monotherapy group (p=0.042).

Discussion and Conclusion: The frequency of seizures during pregnancy is strongly associated with epileptic seizure status in the last year before pregnancy and multiple antiepileptic therapies.

Keywords: Antiepileptic; epilepsy; pregnancy; seizure.

Epilepsy is defined as a common neurological condition characterized by abnormal brain activity with varying degrees of symptoms, including recurrent unprovoked seizures^[1-3]. It is estimated that approximately 15 million women diagnosed with epilepsy worldwide are of child-bearing age^[3]. The prevalence of epilepsy in pregnant women, the most common neurological disease after migraine during pregnancy, is estimated to be 0.3–0.7%^[4-6].

In addition to epileptic seizures, antiepileptic drugs used in the treatment may significantly affect both the mother and the fetus during pregnancy. It has been reported that

the risk of miscarriage due to seizures, preterm birth, gestational hypertension, preeclampsia, fetal growth restriction (FGR), postpartum bleeding, and cesarean section rates is higher in epileptic, pregnant women than in normal pregnant women^[6]. Considering the neonatal outcomes of pregnant women with epilepsy, it has been reported that stillbirth, neonatal/perinatal death, hemorrhagic disease of the newborn, low APGAR score, low birth weight, premature birth, and congenital malformations are more common^[7]. At present, available evidence seems insufficient to show the relationship between epilepsy and adverse pregnancy outcomes and the contribution of antiepileptics to it^[6].

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This study aimed to retrospectively evaluate the perinatal outcomes of pregnant women diagnosed with epilepsy followed in our clinic.

Materials and Methods

In this retrospective cohort study, a total of 58 pregnant women diagnosed with epilepsy who were delivered after pregnancy follow-up at Sakarya University Training and Research Hospital Gynecology and Obstetrics Clinic between January 2015 and March 2021 were evaluated. The ethics committee approval was received from Sakarya University Scientific Research Ethics Committee (Ethics Committee No: 30.03.2021-E71522473-050.01.04-21470-227).

Cases diagnosed with epilepsy by specialist neurologists were included in the study. The data of the patients were obtained from the patient files and electronic records in the hospital archive. Demographic characteristics such as maternal age, gravida, and parity, the time of the last epileptic seizure before pregnancy, and folic acid use before and during pregnancy were evaluated. In addition, the time and frequency of epileptic seizures during pregnancy and the antiepileptic drugs used during pregnancy were recorded. Delivery types, birth weeks, newborn birth weight, and Apgar scores at 1st and 5th min were examined. In addition, obstetric complications, preterm birth, FGR, intrauterine fetal death, neonatal death, and early neonatal complications were examined. Preterm birth was defined as "delivery before 37 weeks of gestation." FGR was defined as "below the 10th percentile weight according to the gestational week in a single fetal growth curve."

Statistical analyzes were performed using the SPSS 24.0 package program (SPSS Inc. and Lead Tech. Inc. Chicago. USA). In numerical data, the distribution of patients was analyzed with the Kolmogorov-Smirnov test. Mann-Whitney U test was used when there was no normal distribution. Chi-square and Fisher's exact test were used for cat-

egorical variables. The results were considered statistically significant when the 95% confidence interval and $p < 0.05$. Descriptive statistics (mean, standard deviation, minimum, and maximum) were given for numerical variables, and frequency distributions (number and percent) for categorical variables.

Results

The demographic and clinical characteristics of the patients are shown in Table 1. The mean age of the patients was 28.4 ± 5.7 years. It was determined that 87.9% of the cases used folic acid in the pre-pregnancy period and during pregnancy. It was determined that the last epileptic seizure before pregnancy occurred within the past 1 year in 39.7% of the cases and 1 year or longer in 60.3% of the cases.

The characteristics of the patients who had seizures during their pregnancy are shown in Table 2. It was determined that 25 cases (43.1%) had seizures during pregnancy. It was determined that epileptic seizures occurred most frequently in the first trimester during pregnancy. It was determined that 29 (87.9%) of 33 cases who did not have seizures during

Table 2. Characteristics of patients with seizures during pregnancy

	n
Epileptic seizure frequency	
1 time	7
Two times	9
Three times	3
More than 3	6
Pregnancy period of epileptic seizure	
First trimester	12
Second trimester	2
Third trimester	2
Every 3 trimesters	9

n: Number.

Table 1. Demographic and clinical characteristics of the patients

Parameters	Minimum	Maximum	Mean	SD
Maternal age (years)	18	41	28.4	5.7
Gravida (number)	1	6	2.5	1.3
Parity (number)	0	3	1	0.9
Gestational age at birth (weeks)	26.4	41.7	38.3	2.2
Birth weight (g)	900	4400	3125	598
1 st min Apgar score	5	9	8.7	0.7
5 th min Apgar score	7	10	9.8	0.6

SD: Standard deviation.

pregnancy had their last seizure more than 1 year before pregnancy, and 4 (12.1%) had their last seizure within the past 1 year before pregnancy. It was determined that 23 patients had seizures in the past 1 year before pregnancy, and 19 (82.6%) of them had seizures during pregnancy. Among 35 patients who had their last seizure before pregnancy for more than 1 year, only 6 (17.1%) patients were found to have seizures during pregnancy. It was determined that the rate of seizures during pregnancy in those who had a seizure in the past 1 year before pregnancy was statistically significantly higher than those who had their last seizure longer than 1 year ($p=0.000$).

The distribution of antiepileptic drugs used during pregnancy is shown in Table 3. The comparison of parameters such as epileptic seizure observed during pregnancy, delivery type, and newborn birth weight between the antiepileptic monotherapy and polytherapy groups is shown in Table 4. It was determined that 17 (68%) of 25 cases who had epileptic seizures during pregnancy received monotherapy and 8 (32%) received polytherapy. It was found that 72.7% of the patients in the polytherapy group had epileptic seizures during pregnancy, and this rate was significantly higher than the monotherapy group ($p=0.042$).

Table 3. Distribution of antiepileptic drugs used in pregnancy

Antiepileptic drugs	n	%
Carbamazepine	13	22.4
Carbamazepine+Levetiracetam	3	5.2
Lamotrigine	19	32.8
Carbamazepine+Lamotrigine	5	8.6
Carbamazepine+Lamotrigine+Levetiracetam	1	1.7
Lamotrigine+Levetiracetam	1	1.7
Levetiracetam	15	25.9
Levetiracetam+Oxcarbazepine	1	1.7

n: Number.

Table 4. Comparison of monotherapy and polytherapy groups

Parameters	Monotherapy	Polytherapy	p
Seizures during pregnancy			0.042
No seizures	30	3	
Seizures	17	8	
Type of delivery			0.450
Vaginal delivery	11	4	
Cesarean section	36	7	
Birth weight (g) (Mean±SD)	3096±613	3247±536	0.372

SD: Standard deviation.

The mean delivery week was 38.3 ± 2.2 weeks, and the mean birth weight was 3125 ± 598 g. It was observed that 74.1% of the cases gave birth by cesarean section. Indications for cesarean section; previous uterine scar in 23 cases (53.5%), epilepsy in 11 cases (25.6%), cephalopelvic disproportion in 3 cases (7%), fetal distress in 4 cases (9.3%), FGR in 1 case (2.3%), and 1 case (2.3%) preeclampsia. It was determined that 4 cases delivered by cesarean section due to fetal distress had more than three seizures in every three trimesters during pregnancy. There was no statistically significant difference in delivery type and birth weight between those who received monotherapy and polytherapy ($p=0.450$, $p=0.372$, respectively).

Considering the obstetric complications, gestational diabetes mellitus (GDM) was observed in 1 case (1.7%), preeclampsia in 1 case (1.7%), FGR in 2 cases (3.4%), and preterm delivery in 4 cases (6.9%). It was observed that neonatal intensive care was needed in 2 cases, one of whom was diagnosed with preeclampsia and delivered preterm delivery. The baby of the case who had preterm delivery was lost in the early neonatal period. It was determined that 2 cases with FGR and 2 of those who gave preterm delivery had seizures in the past 1 year before pregnancy. Intrauterine fetal death was not detected in any of the cases.

Discussion

According to the results of our study, it was found that 56.9% of women diagnosed with epilepsy did not have epileptic seizures during pregnancy. The rate of having epileptic seizures during pregnancy was statistically significantly higher in those who had seizures in the past 1 year before pregnancy than those who had seizures longer than 1 year. In addition, the rate of cases who had epileptic seizures during pregnancy was statistically significantly higher in the polytherapy group than the monotherapy group.

Epilepsy is one of the most common chronic diseases of childbearing age and causes concerns and fears about pregnancy in women. The risk of epileptic seizures during pregnancy, changes in seizure frequency, and difficulties in estimating the effects of epileptic seizures complicate the management and treatment of these patients. When we look at the literature, many studies evaluate the seizure-free period and the frequency of seizures during pregnancy. In one study, epileptic seizures were not observed in 38.3% of the patients during pregnancy, while an increase in seizure frequency was observed in 25.9%, a decrease in 30.9%, and no change in 43.2% of those who had seizures compared to pre-pregnancy^[8]. In another prospective study, epilep-

tic seizures were not observed in 30.9% of the 105 patients evaluated during pregnancy, but in those who had seizures, the frequency of seizures increased in 28.7%, decreased in 25.5%, and remained unchanged in 14.9% compared to the pre-pregnancy period^[9]. Özdemir et al.^[10] stated in their study that 30.87% of the patients did not have epileptic seizures during pregnancy. In the prospective study of Battino et al.,^[11] 3806 pregnant women were evaluated, and epileptic seizures were not observed in 66.6% of these pregnancies. In our study, while the frequency of seizures during pregnancy was not evaluated compared to the pre-pregnancy period, it was found that epileptic seizures were not observed in 56.9% of pregnancies. These differences between studies may be due to the number of patients and different management of the disease.

Pregnancy management of cases whose disease was under control before pregnancy is more manageable, and such cases can show a better clinical course. It is reported that the seizure-free period of the past 1 year before pregnancy is the best indicator that can reflect the frequency of seizures in pregnancy^[12]. Vajda et al.^[13] reported that the risk of having an epileptic seizure during pregnancy was reduced by 50–70% if the year before pregnancy was seizure-free. Özdemir et al.^[10] observed that 78.26% of the patients who did not have seizures during pregnancy did not have seizures in the last 1 year. In another study, it was stated that not having a seizure until 9 months before pregnancy predicted a high probability of 84–92% not to have seizures during pregnancy^[14]. In our study, similar to the literature, it was found that a high rate of 87.9% of those who did not have seizures during pregnancy did not have a seizure in the past 1 year before pregnancy.

Although the exact cause of any increase in seizures during pregnancy in epilepsy patients is unknown, it is likely to be multifactorial. Due to pregnancy, physiological and endocrine changes can lower the seizure threshold and cause seizures by reducing serum levels by changing the pharmacokinetics of antiepileptics^[12]. During pregnancy, patients are advised to continue antiepileptic drugs to reduce maternal and fetal trauma that may occur due to seizures. The aim is to control seizures by avoiding polytherapy with the lowest possible drug dose^[8,12]. Reisinger et al.^[15] found that the probability of worsening epileptic seizures during pregnancy was higher in the polytherapy group than in the monotherapy group. In another study, the incidence of seizures during pregnancy was found to be higher in the polytherapy group than in the monotherapy group^[16]. Similarly, in our study, the rate of seizures in the polytherapy group was higher than in the monother-

apy group. Patients receiving polytherapy already had more severe diseases may have resulted in higher seizure rates in this group.

Another critical point in our study was that four cases delivered by cesarean section due to fetal distress had more than three seizures in every three trimesters during their pregnancy. Özdemir et al.^[17] compared patients with a history of five or more epileptic seizures during pregnancy with patients without epilepsy and patients with epilepsy without a history of seizures during pregnancy. Although there was no statistical difference between the groups, they found umbilical arterial blood pH values lower, partial carbon dioxide pressure values higher, and partial oxygen pressure values lower in patients with a history of 5 or more seizures^[17]. Although umbilical arterial blood gas analysis was not performed in our study, it is not surprising that fetal oxygenation is impaired due to maternal adverse conditions in patients who had a large number of seizures during pregnancy. However, studies with more patients designed with objective criteria are needed to prove this.

Epilepsy cannot be considered an indication for cesarean delivery unless a seizure occurs during labor or the patient is uncooperative^[18]. In the study conducted by Özdemir et al.,^[10] the rate of cesarean delivery was 79.2%, and the rate of pregnancy terminated by cesarean section with the recommendation of a neurologist as a result of frequent seizures during pregnancy was reported as 33.05%. Another study stated that while there was a higher cesarean section rate in epileptic pregnant compared to the control group (65% and 24.9%, respectively), seizures during pregnancy caused a higher cesarean section rate.^[19] In addition, it was stated that the fear that the birth might trigger the seizure and lead to further complications also contributed to the high cesarean rate.^[19] Vajda et al.^[20] stated that the presence of an epilepsy diagnosis on its own contributed to the high elective cesarean section rate. Our study found that 74.1% of the cases were delivered by cesarean section and the rate of patients who had an elective cesarean delivery due to epilepsy was 25.6%.

In the literature, it is seen that the results of the studies on the obstetric or neonatal outcomes of epileptic pregnancy differ from each other. Allotey et al.,^[21] in their meta-analysis in which they examined the global variations of pregnancy complications in epileptic women, stated that factors such as interregional geographic and economic factors, being followed by a neurologist, and access to appropriate treatment may affect obstetric outcomes. In our study, GDM was found in 1 case (1.7%), preeclampsia in 1

case (1.7%), FGR in 2 cases (3.4%), and preterm delivery in 4 cases (6.9%). Due to the limited number of cases and the lack of a control group in our study, it is impossible to comment on the increase in these obstetric outcomes compared to the low-risk population.

There are several limitations of this study. First, it is a retrospective study. Second, due to the absence of a control group, adequate comparisons could not be made between the healthy group and the patient group. However, these problems can be overcome with multicenter prospective studies among larger patient groups.

Conclusion

The frequency of seizures during pregnancy is strongly associated with epileptic seizure status in the last year before pregnancy and multiple antiepileptic therapies. These data may be helpful when providing preconception counseling to epileptic women planning a pregnancy of childbearing age.

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