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ORIGINAL ARTICLE

# Obstetric results of epileptic pregnant women: A retrospective analysis

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## ABSTRACT

**Objective:** Epilepsy is one of the most common neurological diseases on a global scale and the second most common neurological disease during pregnancy. The aim of our study is to evaluate the pregnancy outcomes and complications of pregnant women diagnosed with epilepsy followed in our clinic.

**Material and Methods:** Between March 2018–2022, 147 pregnant women who were followed up in our hospital and diagnosed with epilepsy were examined. Demographic and clinical findings of all patients were compared retrospectively according to drug use history and seizure frequency during pregnancy.

**Results:** There was no significant difference in mean birth weight and mean week of birth according to drug use groups (p=0.385, p=0.115, respectively). There was no significant difference between the drug use groups in terms of the presence of spontaneous abortion and history of preterm birth (p=0.360, p=0.210, respectively). No significant relationship was found between seizure frequency and seizure type (p=0.245). No significant relationship was found between seizure frequency and antiepileptic drug use (p=0.640). The average age of pregnant women with a history of polytherapy was 32.6±8.4 and was found to be significantly higher than the other groups (p=0.042). When the groups were evaluated according to drug use history, it was seen that the duration of epilepsy was significantly longer in the polytherapy group (p=0.044). When the groups were evaluated according to drug use history, it was seen that the cesarean section rate was significantly higher in the polytherapy group (p=0.038).

**Conclusion:** Today, we think that pregnant women diagnosed with epilepsy have a high probability of giving birth to a healthy baby, spontaneous miscarriages are not more common than expected, and there is no significant difference between birth weight or week of birth and the treatment applied during pregnancy. The study also shows that with an appropriate approach and follow-up, it is possible to achieve positive results similar to those in the general population.

**Keywords:** Antiepileptic drugs, epilepsy, pregnancy.

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## INTRODUCTION

Epilepsy is one of the most common neurological diseases that affects 2% of the population on a global scale[1] as the second most common neurological disease in pregnancy after migraine, and a total of 18 million women have epilepsy in the World.[2] Pregnancy is an important decision process for women who have epilepsy. A balance must be established between the risks to the mother and fetus of uncontrolled seizures during pregnancy and the potential teratogenic effects of antiepileptic drugs (AEDs).[3] When an epileptic woman becomes pregnant, there are fetal or maternal risks of epilepsy during pregnancy, the medical treatment used, and the epileptic seizure.[4] Pregnancy also has effects on epilepsy and the AEDs used. There are studies in the literature reporting increased risks of miscarriage, premature birth, intrauterine infant death, intrauterine growth retardation, and long-term mental and psychomotor retardation in the newborn in cases of epilepsy and pregnancy.[5] Counseling before pregnancy, a correct and effective birth control method, and a planned pregnancy will allow the regulation of antiepileptic drugs, minimizing the related risks with folic acid prophylaxis in terms of fetal malformations and especially neural tube defects, and explaining the effects of epilepsy and epilepsy on pregnancy to the family.[6] It can be recommended for most women who have epilepsy to become pregnant because the malformation rates determined by recent studies are not significantly different from the general population.[7] In the treatment of epilepsy during pregnancy, the most critical point is to maintain the balance between control of maternal seizures and teratogenic risk.[8] Although AEDs increase the risk of major and minor congenital anomalies, the risk is lower than considered, and the majority of women who have epilepsy can give birth to healthy babies.[9] In the study conducted by Razaz et al.[10] in which 3586 epileptic pregnant women were examined, it was reported that AED use did not increase the risk of pregnancy and perinatal complications, except for a higher rate of labor induction. Although several studies report that seizures that develop in the first trimester increase the risk of malformations, there are also other studies reporting contrary outcomes.[11] Pregnancy complications such as hyperemesis gravidarum, vaginal bleeding, preeclampsia, eclampsia, vitamin D and K deficiencies, megaloblastic anemia because of decreased folate, premature birth, and postpartum bleeding are more common in epileptic women.[12] When the effects of pregnancy on epilepsy are evaluated, it is seen that seizures increase by approximately 25%.[13] The increase in seizure frequency occurs mostly at the end of the first trimester or the beginning of the second trimester[14] and the increase in seizure frequency during pregnancy is multifactorial. Drug incompatibility, decreased serum AED levels because of changes in the absorption and metabolism of the drug, sleep deprivation, and stress can be listed among the reasons for this.[9] The risk of hypertensive diseases and long-term hospitalization also increases in epileptic pregnant women. In the study conducted by Huang et al.[15] it was reported that abortion, bleeding during pregnancy, postpartum hemorrhage, hypertensive diseases, labor induction, cesarean section, preterm labor, and intrauterine growth retardation were seen at higher rates in epileptic pregnant women. In our study, the purpose was to present pregnancy outcomes and possible complications in pregnant epileptic patients followed in our pregnancy clinic.

## MATERIAL AND METHODS

The study had a retrospective cross-sectional design and was conducted following the principles of the Declaration of Helsinki. Informed consent forms were obtained from the patients. The study was started after receiving ethics committee approval number 2023/209 from our hospital's ethics committee. The files of a total of 147 pregnant women who were diagnosed with epilepsy who applied to our hospital between March 2018 and March 2022 and whose pregnancy follow-ups were performed in our hospital were examined retrospectively. Demographic characteristics of all patients such as age, parity, week of birth, birth weight, 1$^{st}$ and 5$^{th}$ minute Apgar scores, types of epilepsy, and duration of epilepsy were evaluated retrospectively along with fetal malformations, abortion, premature birth, intrauterine growth retardation, antenatal and neonatal problems. Births after the 37$^{th}$ week were categorized as term birth, between 34 and 37 weeks as late preterm birth, and births under the 34$^{th}$ week were categorized as early preterm birth. The distinction of major anomalies from minor anomalies was made in line with the EUROCAT Guideline used in the evaluation of congenital anomalies. It was evaluated whether the patients had an attack during pregnancy. Quantitative data of the patients were reported as mean±standard deviation (SD) (minimum–maximum). Whether there was a relationship between the categorical variables was evaluated with the Chi-Square Test, and whether there was a difference between the independent groups was evaluated with the One-Way Analysis of Variance Test. The results were evaluated with a 95% Confidence Interval (CI). The p-value considered statistically significant was <0.05. The analyses were made with SPSS version 26.0 (IBM Inc., Chicago, IL, USA).

## RESULTS

The mean age of the 147 patients who were evaluated in the study was 31.8±8.8 years. The mean parity of 130 patients with ongoing pregnancy was 1.6±0.5, birth week was 37±2.1, birth weight was 2960±752 g, 1$^{st}$ minute Apgar score was 8.1±0.8, and 5$^{th}$ minute Apgar score was 8.6±0.7. Among 147 pregnant women, 17 (11.5%) had a spontaneous abortion, 108 (73.4%) gave birth in the term period, 15 (10.2%) gave birth in the late preterm period, and 7 (4.7%) gave birth in the early preterm period. In addition, 80 (61.5%) pregnant women had a cesarean section and 50 (38.5%) had a normal spontaneous vaginal birth. The mean duration of epilepsy was 16.8±7.8 years. The average age of pregnant women with a history of polytherapy was found to be 32.6±8.4 years, which was significantly higher than the other groups (p=0.042). No significant difference was found between the groups in terms of parity number according to drug use history (p=0.850). Among the women included in the study group, the mean birth weight of those who did not receive any treatment during pregnancy was 3080±592 g, the mean birth weight of patients who had a history of monotherapy was 2960±505 g, and the mean birth weight of patients who had a history of polytherapy was 2820±610 g, and no significant differences were found between the groups (p=0.385). The mean birth week of women who did not receive any treatment during pregnancy was 38±1.9, the mean birth week of patients with a history of monotherapy was 37±1.9, and the mean week of birth of patients with a history of polytherapy was 36±2.4, and no significant differences were detected between the groups (p=0.115). No

**Table 1: The relationship between treatment history and pregnancy outcomes**

| | Monotherapy | Polytherapy | Not receiving treatment | Total | p |
|---|---|---|---|---|---|
| Age, Mean±SD | 30.5±7.9 | 32.6±8.4 | 30.2±8.1 | 31.8±8.8 | 0.042 |
| Parity, Mean±SD | 1.6±0.6 | 1.5±0.7 | 1.6±0.6 | 1.6±0.5 | 0.850 |
| Birth weight (g), Mean±SD | 2960±505 | 2820±610 | 3080±592 | 2960±752 | 0.385 |
| Birth week, Mean±SD | 37±1.9 | 36±2.4 | 38±1.9 | 37±2.1 | 0.115 |
| 1st minute Apgar score, Mean±SD | 8.1±0.6 | 8.1±0.5 | 8.2±0.6 | 8.1±0.8 | 0.770 |
| 5th minute Apgar score, Mean±SD | 8.7±0.6 | 8.6±0.5 | 8.6±0.5 | 8.6±0.7 | 0.640 |
| Spontaneous abortion, n (%) | 5 (29.4) | 5 (29.4) | 7 (41.1) | 17 (11.5) | 0.360 |
| Duration of epilepsy (year), Mean±SD | 15.5±7.5 | 18.1±6.1 | 15.5±7.7 | 16.8±7.8 | 0.044 |
| Birth type, n (%) | | | | | 0.038 |
| C/S | 44 (68.7) | 18 (78.2) | 18 (41.8) | 80 (61.5) | |
| NSPD | 20 (31.3) | 5 (21.8) | 25 (58.2) | 50 (38.5) | |
| Birth period, n (%) | | | | | 0.210 |
| Term birth | 59 (50) | 18 (15.3) | 41 (34.7) | 108 (73.4) | |
| Late preterm birth | 3 (50) | 2 (33.3) | 1 (16.7) | 15 (10.2) | |
| Early preterm birth | 2 (33.3) | 3 (50) | 1 (16.7) | 7 (4.7) | |

SD: Standard deviation; NSPD: Normal spontaneous perineal birth; C/S: Cesarean delivery.

significant difference was found between the groups in terms of 1st minute and 5th minute Apgar scores according to drug use history (p=0.770, p=0.640 respectively). Among the 17 patients who had a history of spontaneous abortion, 5 (29.4%) pregnant women had a history of monotherapy, 5 (29.4%) pregnant women had a history of polytherapy, and 7 (41.1%) pregnant women did not have any treatment history, and no significant differences were detected between the groups (p=0.360). When the groups were evaluated according to drug use history, the duration of epilepsy was found to be significantly higher in the polytherapy group (p=0.044). When the groups were evaluated according to drug use history, it was found that the cesarean section rate was significantly higher in the polytherapy group (p=0.038). Among the 130 pregnant women who gave birth live, 64 (49.2%) had a history of monotherapy, 23 (17.6%) had a history of polytherapy, and 43 (33%) patients did not receive any treatment. The number of pregnant women who gave birth at term was 118, 59 (50%) of the women in this group were in the monotherapy group, 18 (15.3%) were in the polytherapy group, and 41 (34.7%) pregnant women did not receive any treatment during pregnancy. The number of pregnant women who gave birth in the late preterm period was 6, 3 (50%) of them were in the monotherapy group, 2 (33.3%) were in the polytherapy group, and 1 (16.7%) pregnant woman did not receive any treatment during pregnancy. The number of pregnant women who gave birth in the early preterm period was 6, and 2 of the women (33.3%) in this group were in the monotherapy group, 3 (50%) were in the polytherapy group, and 1 (16.7%) pregnant woman did not receive any treatment during pregnancy, and no significant differences were detected between the groups (p=0.210) (Table 1).

Although 94 (63.9%) women included in the study group had at least one epileptic seizure during pregnancy, no seizures were detected in 53 (36.1%) women. Additionally, 50 (34%) patients in the study group did not use medication during pregnancy, 69 (46.9%) patients had a history of monotherapy, and 28 (19.1%) patients had a history of polytherapy. An increase in seizure frequency was de-

**Table 2: The epilepsy prognosis of the patients**

| | n | % |
|---|---|---|
| Number of seizures | | |
| ≥1 | 94 | 63.9 |
| 0 | 53 | 36.1 |
| Drug history | | |
| Monotherapy | 69 | 46.9 |
| Polytherapy | 28 | 19.1 |
| No treatment | 50 | 34 |
| Seizure prognosis | | |
| Increasing | 40 | 27.2 |
| Decreasing | 50 | 34 |
| No change | 57 | 38.7 |
| Seizure period | | |
| 1st trimester | 15 | 10.2 |
| 2nd trimester | 20 | 13.6 |
| 3rd trimester | 12 | 8.1 |
| 2 separate trimesters | 13 | 8.8 |
| 1-2-3rd trimesters | 24 | 16.3 |

**Table 3: The relationship between seizure prognosis and seizure type and history of epileptic drug use**

| | Increased seizures | | Decreased seizures | | No change | | p |
|---|---|---|---|---|---|---|---|
| | n | % | n | % | n | % | |
| Seizure type | | | | | | | 0.245 |
| Partial | 1 | 7.2 | 7 | 50 | 6 | 42.8 | |
| Generalized | 18 | 21.9 | 28 | 34.2 | 36 | 43.9 | |
| Partial + generalized | 16 | 47 | 9 | 26.5 | 9 | 26.5 | |
| Antiepileptic drug use | | | | | | | 0.640 |
| Monotherapy | 21 | 32.9 | 17 | 26.6 | 26 | 40.5 | |
| Polytherapy | 4 | 17.4 | 12 | 52.2 | 7 | 30.4 | |
| Not receiving treatment | 10 | 23.2 | 15 | 34.9 | 18 | 41.9 | |
| Total | 35 | 26.9 | 44 | 33.8 | 51 | 39.2 | |

tected in 40 (27.2%) women, a decrease in seizure frequency in 50 (34%) women, and no change in seizure frequency was detected in 57 (38.7%) women in the study group. Seizures were reported in 15 (10.2%) pregnant women in the 1st trimester, in 20 (13.6%) pregnant women in the 2nd trimester, in 12 (8.1%) pregnant women in the 3rd trimester, in 13 (8.8%) pregnant women in two separate trimesters, and in 24 (16.3%) pregnant women in all three trimesters (Table 2).

Among the 130 women who gave birth, an increase in seizure frequency was detected in 35 (26.9%) pregnant women during pregnancy, a decrease in seizure frequency in 44 (33.8%) pregnant women, and there were no changes in the seizure frequency in 51 (39.2%) pregnant women during pregnancy in the study group. When the relationship between seizure frequency, seizure type, and antiepileptic drug use was evaluated, no significant relationships were found between the groups (p=0.245, p=0.640, respectively) (Table 3).

## DISCUSSION

The frequency of seizures decreased or remained unchanged during pregnancy in the majority of pregnant women in our study. The period with the lowest seizure frequency was the 2nd trimester. More than half of the patients had a history of seizures at least once during their pregnancy. In our study, the average age of pregnant women with a history of polytherapy was found to be significantly higher. The duration of epilepsy was found to be significantly longer in the polytherapy group, and the cesarean section rate was significantly higher in the polytherapy group. The average age of pregnant women with a history of polytherapy was significantly higher than in other groups. There are conflicting data in the literature in studies evaluating the relationship between age and epilepsy, both in pregnant women and outside the pregnancy period.[16,17] In our study, the high average age in the polytherapy group was associated with the long history of epilepsy in these patients. It has been shown in the literature that the duration of epilepsy is significantly higher in patients receiving multiple drug therapy.[18,19] In our study, it was observed that the duration of epilepsy was significantly longer in the polytherapy group, consistent with the literature. The reason for this relationship can be explained by the fact that patients diagnosed with severe epilepsy have a low remission rate over the years and are resistant to monotherapy.

The mean birth weight and birth week of the women who did not receive any treatment during pregnancy were higher than the mean birth weight and birth week of the infants with a history of monotherapy and polytherapy among the women in the study group, but this difference was not statistically significant. In the study conducted by Pennell et al.,[19] it was reported that the rate of low birth weight and prematurity increased in epileptic pregnant women. In the study conducted by Crawford et al.,[20] it was reported that the rate of premature birth increased in epileptic pregnant women. It is thought that the difference between the literature data and our study is the difference in the number of patients evaluated in the studies and the exclusion criteria. When patients who had a history of spontaneous abortion were evaluated according to their treatment history, no statistically significant differences were detected between those who did not receive medication and those who received polytherapy or monotherapy. In the study conducted by Adab et al.,[21] abortion rates were found to be significantly higher in the epilepsy group. It is thought that the difference between our study and literature data is since spontaneous abortion patients were not hospitalized in our study. Although studies report that complications during pregnancy are more common in pregnant women who have epilepsy, some studies do not support this result. In the study conducted by Annegers et al.,[22] no differences were detected in the rate of spontaneous miscarriage between pregnant women taking and not taking antiepileptic drugs. Although the rate of spontaneous abortion is not known exactly in normal pregnancies, it is reported to be between 10–40%.[23,24] In our study, spontaneous abortion was detected in 17 (11.5%) cases and no significant differences were detected when compared to normal pregnancies. The risk of congenital malformation increases in proportion to the increase in the number and dose of antiepileptic drugs used (i.e., polytherapy and monotherapy).[25] No major anomaly was found in the patients included in our study. A shift towards a higher rate of monotherapy and a change towards the choice of less teratogenic AEDs during the treatment of our patients may have contrib-

uted to the lower risk of malformations. A wide range of results were reported in the study of Mawer et al.,[25] indicating that the frequency of seizures during pregnancy might increase, decrease, or remain unchanged. Similarly, in our study, data regarding the frequency of seizures during pregnancy were found to be compatible with the literature. Although 94 (63.9%) women in the present study group experienced at least one epileptic seizure during pregnancy, no seizures were detected in 53 (36.1%). No increase was detected in seizure frequency in 40 (27.2%) women in the study group, no decrease in seizure frequency in 50 (34%) women, and no change in seizure frequency in 57 (38.7%) women. These findings were found to be compatible with other studies in the literature. No history of status epilepticus during pregnancy was detected in our study group.

The consensus is that there is no change in the frequency of epileptic seizures in most patients. The best indicator that can reflect the frequency of seizures during pregnancy is the frequency of seizures in the past year before the pregnancy.[23] Perhaps the most important factor that affects the increase in epileptic attacks is the discontinuation of drug use during pregnancy.[26] Expectant mothers stop using AEDs (especially in the first 3 months of pregnancy) to avoid the negative effects of the drugs on their children. It was found in the EURAP Study, in which 1736 pregnancies were evaluated, that 58.3% of the patients did not have seizures during pregnancy, 15.9% had a decrease in their seizures, 17.3% had convulsive seizures, and 1.8% had a history of status epilepticus.[27] In our study, the reason for the similar seizure frequency throughout the pregnancy period may be that the patients had regular neurology check-ups. In the study conducted by Schmidt et al.,[13] it was reported that the increase in seizure frequency was more evident in the 1st and 3rd trimesters, but it was reported in the study of Battino et al.[28] that there was a decrease in the frequency of seizures in the 1st trimester. Unlike the literature data, the fewest seizures were observed in our study in the second trimester. The findings of previous studies conducted on cesarean section rates in epileptic pregnant women are variable.[29] In our study, 38.5% of the pregnant women gave birth by normal vaginal birth and 61.5% by cesarean section, and the cesarean rate was observed to be quite high compared to studies in the literature. The high rate of cesarean sections due to patient request in Türkiye reveals the difference between the literature and our study. It was reported in another study that the mean birth weight of newborn infants of epileptic patients was lower than that of controls, but the difference was not at a statistically significant level.[30] AED polytherapy was suggested to be a risk factor for low birth weight compared to monotherapy.[31] In our study, no significant difference was observed in terms of pregnancy outcomes between patients with a history of polytherapy and patients with a history of monotherapy. However, it supports the view that polytherapy is a risk factor for low birth weight. Among the women included in the study group, the mean birth week of those who did not receive any treatment during pregnancy was higher than the mean birth week of those who received monotherapy and polytherapy, but this difference was not at a statistically significant level. The fact that all patients were followed up from a single center throughout their pregnancy is considered a strength of the study. However, the fact that the relationship between drug dose and drug group and perinatal period results in epileptic drug use was not examined can be considered a limitation of the present study.

## CONCLUSION

We think that pregnant women diagnosed with epilepsy have a high probability of giving birth to healthy babies, spontaneous miscarriages are not more common than expected, and there are no significant differences between birth weight or week of birth and the treatment received during pregnancy in the present study. The study also shows that it is possible to obtain positive outcomes almost similar to the general population with an appropriate approach and follow-up.

### Statement

**Ethics Committee Approval:** The Buca Seyfi Demirsoy Training and Research Hospital Non-Interventional Research Ethics Committee granted approval for this study (date: 27.12.2023, number: 2023/209).

**Author Contributions:** Concept – MDU; Design – UA; Supervision – CA; Resource – HAA; Materials – UA; Data Collection and/or Processing – HAA; Analysis and/or Interpretation – UA; Literature Search – MDU; Writing – MDU; Critical Reviews – UA.

**Conflict of Interest:** The authors have no conflict of interest to declare.

**Informed Consent:** Written informed consent was obtained from patients who participated in this study.

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