

## *Outcomes of Pregnancy in Women with Epilepsy in Ardabil*

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### **Abstract**

**Background:** Epilepsy is the second, most common and most dangerous neurological complication that can occur in a pregnant woman. Women with epilepsy (WWE) are at higher risk for miscarriage, prematurity, congenital anomalies and low birth weight (LBW).

**Objectives:** The aim of this study was to investigate the outcome of pregnancy in women with epilepsy.

**Methods:** This descriptive study was conducted on 131 pregnant women with epilepsy who referred to Ardabil Alavi Hospital from September 2019 to September 2021. Necessary information such as BMI, type of seizure, congenital malformation, treatment drug and name of used drugs collected through patients file by a checklist and then analyzed by using statistical methods in SPSS version 25.

**Results:** The frequency of neonate term birth was 83.21% and preterm birth was 16.79%. The frequency of babies with LBW was 22.85%. Most of women with 65.96% had cesarean delivery. More than 83% of seizures were generalized and 67.93% used mono-therapy. Only one fetus had malformation (0.76%). The most frequency among the patients receiving mono-therapy was related to the carbamazepine with 26.71% and among the women treated with multitherapy was related to Levetiracetam plus carbamazepine with 12.97%.

**Conclusion:** Pregnancies with epilepsy, even in cases with multidisciplinary care and no other risk factors, are still significantly associated with higher adverse outcomes.

**Keywords:** *epilepsy, seizures, pregnancy, birth defects, malformation*

### **Introduction**

Epilepsy is defined as a brain disorder characterized by an enduring predisposition to generate epileptic seizures, with cognitive, neurobiological, psychological, and social consequences and can cause cognitive, neurobiological and psychosocial abnormalities in the suffering individuals [1,2]. Most of Seizures occurred in more than half of the women with epilepsy and were more common in third trimester and postpartum. Rates of hypertensive

disorders, caesarean deliveries, low birth weight and congenital malformations were high [3]. The prevalence of epilepsy in adults is 1.65% and occurred about 1 out of every 200 pregnancies. After headache, epilepsy is the second most common and dangerous neurological complication that can occur in a pregnant woman. Although it is known that both estrogen and progesterone are effective in seizure activity but its relationship with pregnancy is not clearly stated yet. Women with epilepsy are at higher risk

for miscarriage, prematurity, congenital anomalies and low birth weight. During pregnancy, epilepsy remains stable in about 46% of people and with increasing or decreasing change in rest of pregnant women [4].

Various obstetric complications such as caesarean section, miscarriage, preterm birth, antepartum and postpartum hemorrhage, and maternal death have been reported more frequently in women with epilepsy than in the general population and prevalence of congenital abnormalities such as cleft lip and palate, heart defects, defects in the formation of the nerve cord, skeletal abnormalities and hypospadias in neonates who were exposed to anti-epileptic drugs during their embryonic period is 2 to 3 times more than other neonates [5,6,7].

Most of WWE require ongoing medical therapy with antiepileptic drugs (AEDs) during pregnancy and most of them are at risk of adverse pregnancy outcomes. [8]

Due to significant variation in many prospective and retrospective reported data across countries, ethnicities, geographical locations and socioeconomic status and by considering that each population group should have its own data on pregnancy and neonatal outcomes among WWE, this is the first study reporting pregnancy and neonatal outcomes in Ardabil WWE and so, the aim of this study was to report pregnancy, delivery and neonatal outcomes in women with epilepsy.

### Methods

This is a descriptive study that has been done on all 131 pregnant women which their epilepsy confirmed before by a neurologist using an electroencephalogram (EEG) referred to Alavi

Hospital in Ardabil city. The sampling method was census and we included all pregnant women with epilepsy from September 2019 to September 2021.

Necessary information were completed of patients hospital files by a checklist which including mother's age during pregnancy, mother's height, mother's weight before pregnancy, mother's occupation, mother's level of education, gestational age, type of delivery, complications of pregnancy, frequency of repeated seizures during pregnancy, congenital malformation, having control on seizure, low birth weight (<2500 g), type of seizure, type of anticonvulsant treatment (mono or multiple), status epilepticus in pregnancy and the time of the last seizure before pregnancy and in the cases needed more explanation in addition to their files, the other required information were collected through telephone calls and interviews. All women in this study had confirmed epilepsy by a neurologist and women with diseases other than epilepsy were not included from the study. Collected data were analyzed by SPSS version 25 and frequencies were reported as numbers and percentages, continuous data as means with standard deviations.

### Results

The frequency of term birth was 109 with 83.21%. Among all neonates, 26 (19.81%) were overweight. 30.87% of women were seizure-free during pregnancy. 65.96% of the women delivered by caesarean section and the majority delivered in term. Major congenital malformation (MCM) was diagnosed in only one fetus (Table 1).

**Table 1: Frequency of Pregnancy Outcomes in the Women**

Variables	n	%	
<b>Neonate gestational age</b>	Preterm birth	22	16.79
	Term birth	109	83.21
<b>Birth weight (gr)</b>	LBW (less than 2500)	30	22.85
	Normal (2500 to 3500)	75	57.34
	Overweight (more than 3500)	26	19.81
<b>delivery method</b>	Vaginal delivery	36	27.81
	Cesarean section	87	65.96
	Spontaneous abortion	5	4.03
	D & C	3	2.2
<b>Epilepsy type</b>	Focal	22	16.78
	Generalized	109	83.22
<b>Epilepsy therapy in pregnancy</b>	No AEDs	18	13.74
	Monotherapy	89	67.93
	Multitherapy	24	18.32
<b>Seizures attacks during pregnancy</b>	No	40	30.87
	Yes	91	69.13

The Mean (SD) age of women at the time of delivery was 26.14 (5.67) years which most of them (42.75%) were in the age group of 25 to 30. Of all women, 39.9% were overweight. The average pre-pregnancy weight of the participants was 74.5 kg, their average height was 161.2 cm, and the overall average body mass index (BMI) was 29.22. Most of women had primary education (23.6%).

Of all women with generalized seizures, 92 (84.6%) were tonic clonic, 10 (9.1%) were myoclonic and rest of them were Absence with 7 (6.3%).

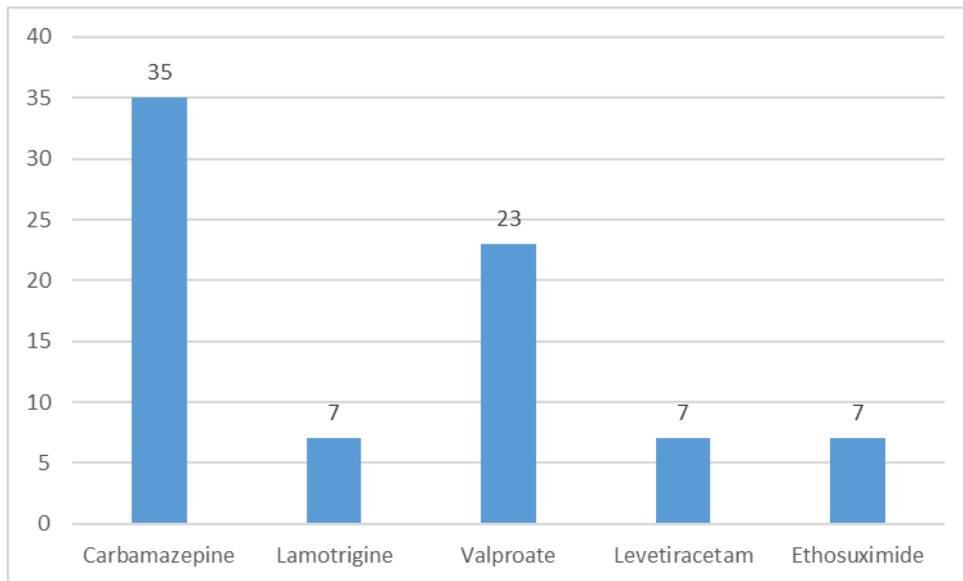
Of all women, 40.78% were experienced seizures five times or more during pregnancy. The lowest frequency belonged to people with Status Epilepticus with 1.91%. Most of women had seizures in the first, second and third trimesters (39.80%) (Table 2).

**Table 2: Frequency of Information Related to the Number and time of Seizure Attacks in Female Subjects**

Variables	n	%	
<b>Number of attacks during pregnancy</b>	1-2 times	30	34
	three times	19	20.39
	Four times	3	2.92
	Five times and more	37	40.78
	Status Epilepticus	2	1.94
<b>Time of seizure attacks</b>	Only the first trimester	20	25.24
	Only the second trimester	2	1.94
	Only the third trimester	18	21.36
	First and second trimester	3	1.94
	First and third trimester	5	3.88
	Second and third trimesters	4	5.84
	First, second and third trimesters	38	39.8
<b>Fetal abnormality</b>	Cleft palate and lip	1	0.76
	No abnormality	130	99.24

Of all women, 33 (25.2%) had perinatal complications which of them, 20 (60.6%) had Intrauterine Growth Restriction (IUGR), 10 (30.3%) had preterm labor, and 3 (9.1%) had preeclampsia.

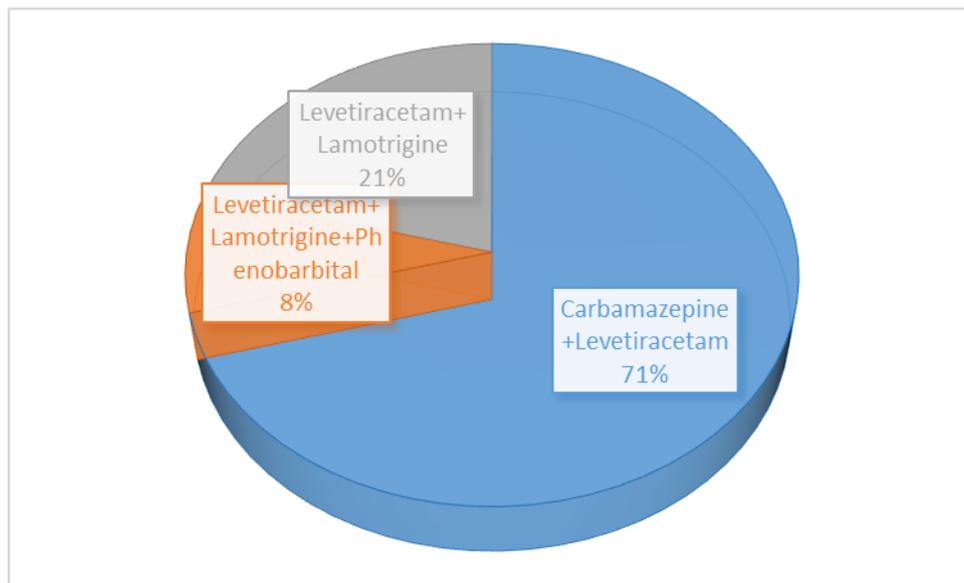
The most used drug for treatment among women who received mono-therapy was related to the Carbamazepine with 26.71% (Figure 1).



**Figure 1: Most commonly Used AEDs (Monotherapy) by Name of Drug**

The most used treatment among women who received multi drugs was related to the

Levetiracetam+ Carbamazepine with 13% (Figure 2).



**Figure 2: Most Commonly Used AEDs (Multitherapy) by Name of Drug**

**Discussion**

The results of this study showed that 83.21% of neonates born to mothers with epilepsy were term and 16.79% were preterm birth. In a study by Basok et al., the rate of term and preterm birth in

WWE were 91.3% and 5.8%, respectively which wasn't in line with our study results and the difference can be related to many factors like the selected cases, inclusion criteria, sample size and other factors [8].

Razaz et al., in a study showed that there is a significant relation between epilepsy and preterm birth outcome and due to non-evaluation of this relation in our study, we cannot confirm this relation in this study and we need for other study to prove it at the future [9].

Melikova and Sun in their studies showed a positive and significant relationship between the incidence of preterm birth with epilepsy and its attacks during pregnancy and in term of term and preterm birth rate and due to non-evaluation of this relation in our study because of our study design, we cannot confirm this relation in this study and we need for other study to prove it at the future [10,11].

In this study we resulted that, 57.34% of neonates had normal weight and 22.85% had Low Birth Weight (<2500 g) which was in line with Soontornpun et al., study because they showed in a cohort study entitled “Pregnancy Outcomes Among Women with Epilepsy”, the rate of LBW was 19.4% [12]. These data emphasize the necessity of regular monitoring of fetal weight in ultrasound and providing appropriate intervention. The occurrence of 22.85% of LBW in our study may be related to seizures and antiepileptic drugs, and may also be influenced by the socioeconomic status of the mother or other factors in addition to the above causes [13]. Also, Huang et al., in their study showed that pregnant WWE are at high risk of obstetric complications. Women with epilepsy who experience seizures during pregnancy are at high risk of preterm birth and having low birth weight infants [11].

In the present study, most of the mothers (65.96%) terminated their pregnancies by cesarean section, 27.81% by vaginal, 4.03% by spontaneous abortion, and 2.2% by curettage (D & C).

In some studies, similar to our study results most of women with epilepsy terminated their pregnancy with cesarean section and usually choose an elective caesarean section because they are concerned about seizures during labor [8,10].

In the present study, 83.22% of seizures in pregnant mothers with epilepsy were generalized and 16.78% were focal. Also, the results showed that in generalized seizures, the most cases were tonic-colonic. In consistent with other studies, in our study the occurrence of general seizures was more than focal seizures [1,14]

In the study of Basok et al., unlike the present study the rate of focal seizure was more than generalized seizure because in our study the rate of generalized seizure with 83% was more than focal seizure with 17% and these difference can be related to many factors like type of seizure in selected women, number of participants in the study and other clinical factors [8].

In this study, 67.93% of women with epilepsy were treated with monotherapy, 18.32% with multi-therapy and 13.74% of them were with no therapy. In the study by Basok et al., similar to our study results, most of women used monotherapy method [8]. Aydin et al., in a study showed that 59.2% of WWE were treated with mono-therapy and 13.6% with multi-therapy which was in line with our study results [15]. The use of antiepileptic drugs during pregnancy can have teratogenic and long-term neurodevelopmental effects on the fetus and so neurologists and obstetricians must work together to balance the risk of congenital malformations with the need for seizure control. Women with epilepsy are recommended to participate in pre-pregnancy counseling, consultation and planning with their doctors, who should receive the lowest effective dose of anti-epileptic drugs that have minimal fetal toxicity [16].

Among the mothers with epilepsy receiving monotherapy, 26.71% were treated with carbamazepine, 12.97% were treated with levetiracetam, and 12.97% were treated with levetiracetam + carbamazepine. In Bosak et al., study the AEDs were prescribed in the majority of pregnancies (158,92.4%), mainly in monotherapy. The most frequently used AEDs were levetiracetam (LEV) and lamotrigine (LTG). Our study wasn't in line with Bosak et al., study because in our study most of WWE were used Carbamazepine and valproate [8].

In the present study, 74.80% had no perinatal complications and among those who had complications, the most frequency was IUGR with 20 cases, 10 cases were preterm labor and 3 cases were preeclampsia. Studies have shown that women with epilepsy have an increased risk of mild preeclampsia, but not severe preeclampsia. [17].

In this study, most of WWE have seizures attacks during pregnancy (69.13%) which was in line with Bosak et al., and Alshiekh et al., study [1,8].

Malformation rate in this study was very low (0.76%) which was in line with Bosak et al., study with (0.6%). In our study Cleft palate and lip was detected in one foetus and in the Bosak study major congenital malformation (MCM) was detected only in one foetus, and resulted in induced abortion [8]. This finding may be related to the low rate of exposure to highly teratogenic AEDs. However, newborns were not followed later, and data on malformation detected at the age of 12 months was not available so we cannot discuss more.

The present study also contained some limitations. First, as it was a hospital-based study and data extracted from the patients' files and interviews with them at one point in one time, it can be considered that the observed prevalence may not be a true reflection of the whole community. Furthermore, it is highly likely that some women might have not disclosed their epileptic status due to social fear and stigmatization. Thus, it may be difficult to generalize the findings of this study. Second, the statistical power of the analysis may be affected due to the small sample size of the study. Thirdly, our study did not contain a control group.

### Conclusion

This study showed that in women with epilepsy even in cases with multidisciplinary care and no other risk factors who experience seizures during pregnancy, their neonates can be probably at risk of adverse outcomes in the future.

We can have suggested that the education for WWE should be strengthened and counseling for women with epilepsy who contemplate discontinuing their antiepileptic drug treatment during pregnancy should be improved. Also, further studies are needed to find risk factors for adverse pregnancy/neonatal outcomes in Ardabil women with epilepsy.

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### Conflict of interest

The authors declare no conflict of interest.

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