Comparison of Maternal and Fetal Outcomes, In Epileptic and Non-Epileptic Mothers

Abstract

Epilepsy is a neurological disorder requiring medical management during pregnancy which can affect the course of pregnancy, labor, delivery, and fetal development. There have been few reports on obstetric outcomes in pregnant Thai women who have had epilepsy.

Objective: The study was designed to compare maternal and fetal unfavorable outcomes in epileptic and non-epileptic mothers.

Methods: We performed a retrospective study by collecting data from 200 mothers who attended antenatal care and delivery at the Faculty of Medicine Vajira Hospital between January 2017 to 2023.

Result: Two hundred patients' medical records were included in the study. All 12 epileptic mothers (6%) were assigned to the study group. The average age of epileptic mothers was of 26.50 (±6.67) years old which was younger than the non-epileptic group (30.66±7.01 years old) and the BMI on delivery in the epileptic group was 28.23 (±5.24) which was lower than the non-epileptic group (28.31±5.26) with statistically significant. We found 25% of premature birth, fetal low birth weight, and low APGAR score in the epileptic mothers' group which is significantly higher than the non-epileptic group. Moreover, all epileptic mothers who have had valproic acid even in low doses (< 800 mg) were found to have preterm birth and low fetal birth weight.

Conclusion: From our study, epileptic mothers had a higher rate of unfavorable fetal outcomes at birth than non-epileptic mothers which may be associated with valproic acid.

Keywords: Pregnancy, Epilepsy, Maternal and fetal outcomes

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Introduction

Epilepsy is a common neurological disorder characterized by recurrent seizures that affects around 4-10 out of every 1,000 people, and it is the most encountered neurological condition requiring medical treatment during pregnancy.[1] Pregnancy mothers are particularly affected by this disorder, with one in 200 being affected[2] recurrent seizures, with an annual incidence between 40 and 80 per 100,000 worldwide.[3] Additionally, 40% of women with epilepsy are in the reproductive age group, which means that it is a relatively common condition during pregnancy with a prevalence of around 0.3-0.7%.[4] Even though over 90% of women with epilepsy will have good outcomes, however, it can affect the course of pregnancy, labor, delivery, and fetal development.[5,6] It is commonly believed that women with epilepsy have a higher risk of obstetric complications, including low birth weight (LBW), preterm birth (PTB), preterm birth obstetric hemorrhage, perinatal mortality, development delay[7-10] and pre-eclampsia and Eclampsia, abruptio placenta, and increased risk of cesarean delivery have been reported[11,12] but actual data have been conflicting.[2,9] Some authors have demonstrated that there is an increased risk of preeclampsia in women with epilepsy compared with the general population[13-15], whereas others did not report any increase.[16-18] Current guidelines for the treatment of pregnant women with epilepsy emphasize the need for preconception counseling for women with epilepsy, who are contemplating pregnancy. Women of child bearing age should be informed about risks associated with epilepsy and pregnancy, the importance of planned pregnancy, use of lowest effective monotherapy dose that controls seizures.[22] Accordingly, there have

There have been few reports on obstetric outcomes in pregnant Thai women who have had epilepsy. Therefore, we design this retrospective study to compare maternal and fetal unfavorable outcomes in epileptic and non-epileptic mothers who attended antenatal care and delivery at the Faculty of Medicine Vajira Hospital. We are expected that the results of this study will improve treatment outcome for physicians and healthcare professionals caring for epileptic mothers and educate them about pre-pregnancy risks to prevent maternal and fetal loss at the Faculty of Medicine Vajira Hospital

Objective

The primary objective: The purpose of this study was to assess the maternal morbidity, mode of delivery, fetal, and neonatal adverse outcomes in epileptic and non-epileptic mothers.

The secondary objective: To study the mortality rate of mothers and fetal birth during pregnancy in epileptic and non-epileptic mothers.

Methods

1. Study design

We performed a retrospective collecting data of patients available in the system database (EPHIS) for all singleton epileptic mothers who attended antenatal care and delivered at Faculty of Medicine Vajira Hospital from January 2017 to January 2023.

We included all epileptic mothers who were diagnosed before pregnancy, and non-epileptic mothers and divided into two study groups (Group 1), epileptic mothers and (Group 2), non-epileptic mothers. The study was ethically approved by our Institutional Review Board. Both

groups were followed up and delivered in our center during the study period. Patients with unconfirmed diagnosis, multifetal pregnancy, molar pregnancy, death fetus in utero and or lacking prenatal care were excluded from analysis. The mothers who were eligible for enrolment into the non-epileptic group were randomly selected with a Stratified Random Sampling ratio of 1: 57. The medical records of the patients were also reviewed.

Body mass index (BMI) were collected at the third trimester of pregnancy and overweight was defined as BMI greater than 30 kg/m^2

Active epilepsy was defined as those with seizures occurring <2 years before pregnancy and inactive epilepsy was defined as those with seizures 2 years or more before pregnancy regardless of antiseizure medication treatments.

A total of 10796 live births database were reviewed. Of these, 12 births (6%) were to epileptic mothers (Group 1) who fulfilled our inclusion criteria, and were matched with 188 births (94%) to non-epileptic mothers (Group 2), during the same study period.

The number of antiseizure medications (ASM) currently used, type of ASM, number of years since diagnosis and last seizure attack, and the occurrence of seizure activity during pregnancy were recorded and analyzed.

The characteristics of the study groups included women's age, parity, gestational age, height, weight, other comorbidities including; diabetes, high blood pressure, dyslipidemia, gestational diabetes, pregnancy induced hypertension, history of previous lower segment caesarean delivery, history of miscarriage and others are shown in Tables 1.

Characteristics of labor, mode of delivery, post-partum hemorrhage and length of hospital stay are shown in Table 2.

Neonatal outcome: 1- and 5-minute Apgar scores, low birth weight shown in Table 4.

The primary outcomes included the rates of preterm birth (delivery before 37 complete weeks of gestation), LBW (birth weight of <2500 g), and preeclampsia (new onset of hypertension defined as blood pressure ≥ 140/90 mm Hg, plus proteinuria defined as ≥1+ on urinary dipstick or 24-hour urinary protein ≥300 mg after 20 weeks of gestation).

The secondary outcomes included the incidence of other adverse pregnancy outcomes. These included mode of delivery, postpartum hemorrhage, low Apgar score (a score of less than 7 at 1 and 5 min), fetal loss (fetal death after 20 weeks of gestation) and maternal death.

2. Study population

The target population is epileptic and non-epileptic mothers at the Faculty of Medicine Vajira Hospital.

- The inclusion criteria are:

1. Epileptic and non-epileptic mothers who attended antenatal care and delivered at the Faculty of Medicine Vajira Hospital between 1st January 2017 and 1st January 2023.

- The exclusion criteria are:

1. Epileptic and non-epileptic mothers with incomplete record in the EPHIS system or lack of information needed to analyze.

2. Patients refused to provide information.

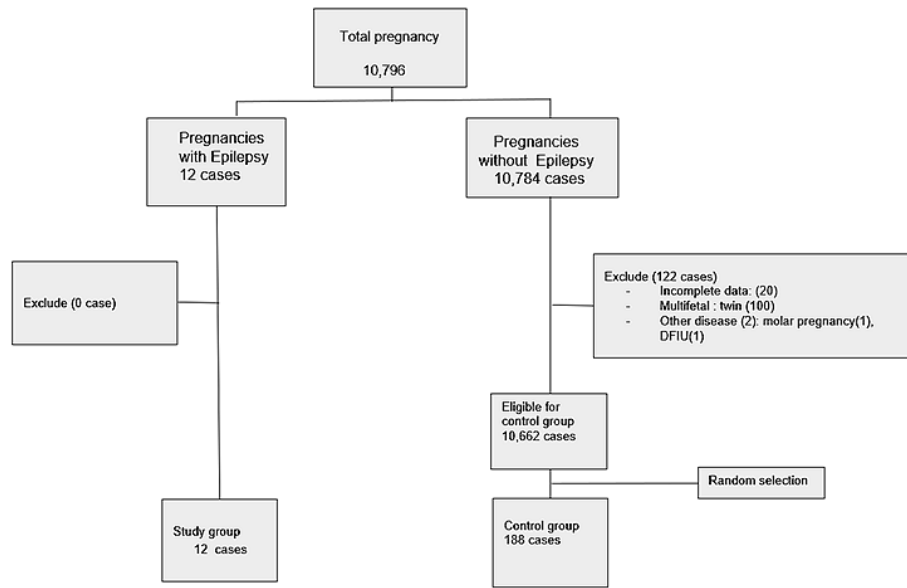3. Patients cannot participate in research activities.

Figure 1 Consort flow diagram

3. Statistical analysis

This study is analytical research with a retrospective study. The analysis and presentation of the data were divided into two parts according to the type of data and specify the statistics used in the analysis to answer the research objectives.

- Descriptive statistics for qualitative data: gender, age, weight, height, body mass index, underlying disease, previous cesarean section history. Number of pregnancies using number, percentage, mean and standard deviation or the median and the minimum and maximum according to the distribution of the data.

- Interferential statistics using multiple logistic regression analysis with paired t-test statistics to find differences between the antenatal history of pregnant patients with epilepsy and without epilepsy and relative risk with 95% confidence interval (CI). P-value <0.05 was considered significant.

Results

1. Baseline characteristics

This study was an inpatient study of mothers receiving antenatal care and treatment at Vajira Hospital from the database in the EPHIS program for research which can analyze the data as follows; 200 patients were included in our analysis. From the data analysis, it was found that the study group (epileptic mothers) had an average age of 26.50 years (±6.67), their body mass index (BMI) was 26.97 (± 4.90), no other disease in addition to epilepsy 41.7%, had single pregnancy 58.3%, during this pregnancy 58.3% had never had a seizure and had a seizure 1 time 33.4%, had a gestational age ≥37 weeks 50.0%. Also, the birth weight of most babies was 2,533.33 g (±969.93) and was delivered by cesarean section and spontaneous labor 50.0%, had complications during pregnancy due to other reasons, separation of episiotomy and caesarean section 25.0%, requiring hospitalization for >3 days 66.7%, during pregnancy, all had to take medicine 100.0% and had the last seizure in the period of 1 year, >1 years and >2 years, equal to 33.3%, as shown in Table 1.

For the analysis, the non-epileptic group (Group2) had a mean age of 30.66 years (±7.01) with a mean weight. 70.13 kilograms (±12.94), mean height 157.44 centimeters (±5.86), mean body mass index (BMI) 28.31 (± 5.26), most of the mothers did

not have other underlying diseases in addition to epilepsy 43.6%, had multiple pregnancies 35.6%, had a gestational age ≥37 weeks 66.5%, and most of the babies' birth weights were 2,987.67 grams (± 552.79), 53.7% of them were delivered by cesarean section. During pregnancy, 60.6% had no complications and hospital stay for >3 days 51.1%. Details are shown in Table 1.

Table 1 Characteristics of the study population (n = 200). Group 1 epileptic mothers, and Group 2 non-epileptic mothers.

Characteristics	Number (percentage)/ average ± standard deviation		*p-value*
	Group 1	Group 2	
Age(y)	26.50 ± 6.67	30.66 ± 7.01	<.001
Maternal weight (kg)	67.67 ± 14.64	70.13 ± 12.94	<.001
Maternal height (cm)	158.00 ± 5.34	157.44 ± 5.86	<.001
Body mass index (BMI)	26.97 ± 4.90	28.31 ± 5.26	<.001
Gestational age (wk)			<.001
- < 36	4(33.3)	31(16.5)	
- 37	2(16.7)	32(17.0)	
- > 37	6(50.0)	125(66.5)	
Underlying diseases			
- No	5(41.7)	82(43.6)	<.001
- Diabetes	2(16.7)	2(1.1)	.039
- Hypertension	1(8.3)	5(2.7)	.019
- Others: thalassemia, hyperthyroid, chronic hepatitis B	4(33.3)	99(52.6)	.568
Type of antiseizure medications (only epilepsy group)			
- Levetiracetam and carbamazepine or phenytoin, or valproic acid	4(33.3)		
- Carbamazepine and valproic acid	4(33.4)		
- Phenytoin or valproic acid alone	4(33.3)		
Seizure free (yr)			.007
- >2 yr	4(33.3)	188(100.0)	
- <2 yr	8(66.7)		

Table 2 Maternal complications for the study groups. Group 1 epileptic mothers, and Group 2 non-epileptic mothers.

Characteristics	Number (percentage)/ average ± standard deviation		*p-value*
	Group 1	Group 2	
Complications			<.001
- No	5(41.7)	61(32.4)	<.001
- Premature birth	3(25.0)	13(6.9)	<.001
- Separation of episiotomy	3(25.0)	5(2.7)	<.001
- Preeclampsia	1(8.3)	16(8.5)	<.001
- Postpartum hemorrhage	0(0)	7(3.7)	<.001
- Gestational hypertension	1(8.3)	26(13.8)	<.001
- Gestational diabetes	0(0)	60(31.9)	<.001
Length of hospital stay (days)	4(33.3)	92(48.9)	<.001
- 1-3	8(66.7)	96(51.1)	.388
- >3			

Table 3 Characteristics of labor and mode of delivery of the study. Group 1 epileptic mothers, and Group 2 non-epileptic mothers.

Mode of delivery	Number (percentage)/ average ± standard deviation		p-value
	Group 1	Group 2	
Mode of delivery			<.001
- Cesarean section	6(50.0)	101(53.7)	
- Spontaneous labor	6(50.0)	80(42.6)	
- Spontaneous labor with assist	0(0)	7(3.7)	

Table 4 Neonatal outcomes for the study groups. Group 1 epileptic mothers, and Group 2 non-epileptic mothers.

Neonatal outcomes	Number (percentage)/ average ± standard deviation		p-value
	Group 1	Group 2	
Birth weight (g)	2,533.33±696	2,987.67±552.7	<.001
Low birth weight (<1500 g)	3(25.0)	4(2.13)	<.001
Apgar			
< 7 (1 min)	2(16.7)	20(10.6)	<.001
<7 (5 min)	1(8.3)	6(3.2)	<.001

2. Outcomes

The baseline clinical characteristic was not different in two groups except higher maternal age and BMI on delivery which was higher in the non-epileptic group as shown in Table 1.

2.1 The incidence of unfavorable neonatal outcomes; preterm birth, low birth weight and low APGAR score was increased in epileptic mothers as shown in Table 4. All three epileptic mothers who have had valproic acid (450 mg/d, 750 mg/d, and 3,000 mg/d) also had unfavorable neonatal outcomes. One epileptic mother who received 1,000 mg of levetiracetam had preterm birth due to preeclampsia but the fetal birth weight was 2,400 gram and had normal APGAR score.

2.2 The maternal complications were not different between the two groups as shown in Table 2.

Discussion

We found that, increasing maternal age and BMI on delivery in non-epileptic group do not affect fetal outcome except the non-epileptic group seems to have significant longer hospital stay. The longer hospital stay may be associated with high number of cesarean sections in the non-epileptic group.

From this study, comparing maternal and fetal outcomes in epileptic and non-epileptic mothers, we found the higher unfavorable fetal outcomes in epileptic mothers as expected, implied that underlying epilepsy may affected the fetal outcome. One issue that may associated with the outcomes was the antiseizure medications.

Among epileptic mothers, 66.7% used ≥ 2 anticonvulsants. It was found that mothers who treated with valproic acid had a higher rate of preterm birth, fetal low birth weight and low APGAR

score even in low dose. However, one epileptic mother who take only levetiracetam also had preterm birth but the fetal outcome was favorable in both birth weight and APGAR score.

The limitation of this study was its retrospective nature, relatively small patient sample size in the epileptic group, and no long-term follow-up. The outcome at birth may not implied the long-term outcome such as cognitive and fetal growth, future prospective studies is required.

Conclusion

In our study, it was established that the risk of fetal complications at birth was higher in epileptic mothers that may be associated with antiseizure medications especially valproic acid. However, the future study needs to be evaluated the long-term fetal outcomes.

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