Original Article

Epilepsy in Pregnancy: Maternal and Fetal Outcomes of Antiepileptic Treatments

Epilepsy in Pregnancy

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ABSTRACT

Objective: To investigate the effects of various AEDs on maternal and fetal outcomes during pregnancy in a cohort of 135 women with epilepsy.

Study Design: A retrospective cohort study

Place and Duration of Study: This study was conducted at the K-health care hospital, Karachi during March 2023 to March 2024.

Methods: The cohort included 135 pregnant women diagnosed with epilepsy. Maternal seizure control, drug adherence, and fetal outcomes (e.g., congenital anomalies, birth weight) were analyzed.

Results: Maternal seizure control was achieved in 68% of patients, with a higher seizure-free rate in those on monotherapy compared to polytherapy. Fetal outcomes varied with the type of AED, with higher rates of congenital anomalies observed in polytherapy groups. Low birth weight was more common in pregnancies exposed to sodium valproate.

Conclusion: The choice of AEDs significantly impacts maternal seizure control and fetal outcomes. Monotherapy regimens, particularly lamotrigine and levetiracetam, were associated with better maternal seizure control and fewer adverse fetal outcomes compared to polytherapy regimens.

Key Words: Epilepsy, Pregnancy, Fetal Outcomes, Antiepileptic Treatments

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INTRODUCTION

Epilepsy is a chronic neurological disorder affecting approximately 50 million people worldwide, with women of childbearing age representing a significant proportion of this population. Pregnancy poses a unique set of challenges for women with epilepsy, as both the disease itself and the treatments required for its management can significantly influence maternal and fetal health. Seizures during pregnancy, particularly generalized tonic-clonic seizures, are associated with increased risks of trauma, placental abruption, status epilepticus, and even maternal mortality[1].

For the fetus, maternal seizures can result in intrauterine growth restriction, preterm birth, stillbirth, and long-term neurodevelopmental impairments, emphasizing the critical importance of maintaining seizure control during pregnancy[2]. The cornerstone of epilepsy management is the use of antiepileptic drugs (AEDs), which effectively reduce seizure frequency and severity. However, AEDs introduce a dual challenge during pregnancy: while they are essential for maintaining seizure control, many AEDs cross the placenta, potentially impacting fetal development. Older-generation AEDs, such as sodium valproate and phenytoin, are associated with higher risks of teratogenic effects, including major congenital malformations (MCMs) such as neural tube defects, cleft palate, cardiac abnormalities, and craniofacial dysmorphism[3]. These risks have been extensively documented in studies showing that the teratogenicity of sodium valproate, for instance, is dose-dependent, with higher doses correlating with increased risks of congenital anomalies[4]. In contrast, newer-generation AEDs like lamotrigine and levetiracetam have demonstrated improved safety profiles. Studies have shown that these drugs are associated with significantly lower rates of MCMs and neurodevelopmental impairments compared to older-generation AEDs. However, even these drugs require close monitoring during pregnancy to avoid complications such as subtherapeutic levels or potential drug-related adverse effects[5].

Physiological changes during pregnancy complicate AED management. Increased renal clearance, reduced

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protein binding, and enhanced hepatic metabolism lead to altered pharmacokinetics for many AEDs. For example, lamotrigine clearance can increase by 200-300% during pregnancy, resulting in decreased serum drug concentrations and an elevated risk of breakthrough seizures[6]. Therapeutic drug monitoring (TDM) has therefore become an essential component of epilepsy management during pregnancy, allowing clinicians to make precise dose adjustments to maintain therapeutic levels without increasing the risk of drug toxicity[7]. The psychosocial challenges faced by pregnant women with epilepsy further complicate management. Many women experience heightened anxiety about the potential teratogenic effects of AEDs and the impact of their condition on fetal health. This anxiety often leads to poor medication adherence, with some women discontinuing AEDs entirely, resulting in an increased risk of uncontrolled seizures. Societal stigma and lack of access to specialized care further exacerbate these issues, emphasizing the need for comprehensive patient education and support system[8]. Preconception counseling has emerged as a cornerstone of epilepsy management for women planning to conceive. This proactive approach allows clinicians to transition patients to safer AED regimens, initiate folic acid supplementation to reduce the risk of neural tube defects, and provide education about the risks and benefits of AED use during pregnancy. Studies have consistently shown that women who receive preconception counseling have significantly better maternal and fetal outcomes compared to others[9]. Despite advancements in epilepsy care, significant gaps remain in understanding the long-term neurodevelopmental effects of AED exposure in utero and the optimal management of refractory epilepsy during pregnancy. This study aims to address these gaps by evaluating maternal and fetal outcomes associated with AED use in a cohort of 135 pregnant women with epilepsy. By comparing outcomes between monotherapy and polytherapy regimens, the study seeks to provide evidence-based insights into safer and more effective treatment strategies for this population[10].

METHODS

A retrospective cohort study was conducted at K-health care hospital, Karachi during March 2023 to March 2024. Data were collected from medical records of 135 pregnant women diagnosed with epilepsy.

Inclusion Criteria:

- Pregnant women aged 18–40 years.
- Diagnosed with epilepsy before pregnancy.
- Receiving AEDs during pregnancy.

Exclusion Criteria:

- Women with other neurological disorders.
- Pregnancies with known chromosomal abnormalities.
- Incomplete medical records.

Data Collection: Clinical data were collected, including demographic information, type of epilepsy, AED regimen (monotherapy or polytherapy), maternal seizure frequency, drug adherence, and fetal outcomes. Outcomes assessed included congenital anomalies, low birth weight (<2.5 kg), preterm birth (<37 weeks), and perinatal mortality.

Statistical Analysis: Data were analyzed using SPSS version 25. Descriptive statistics were used for demographic and clinical variables. Chi-square and t-tests were employed to compare outcomes between AED regimens, with significance set at $p < 0.05$.

RESULTS

The cohort included 135 pregnant women with epilepsy, with a mean age of 29.8 years (±4.6). Focal epilepsy was the most common type, accounting for 62% of cases.

Table No. 1: Patient Demographics and Epilepsy Characteristics

Parameter	Value	Percentage (%)
Total Patients (n)	135	100
Mean Age (years)	29.8 ± 4.6	-
Type of Epilepsy		
- Focal Epilepsy	84	62
-Generalized Epilepsy	51	38
AED Regimen		
- Monotherapy	88	65
- Polytherapy	47	35

Maternal seizure control was achieved in 68% of patients, with a higher rate of seizure-free pregnancies in the monotherapy group (78%) compared to the polytherapy group (49%).

Table No. 2: Maternal Outcomes by AED Regimen

Outcome	Monotherapy (n = 88)	Polytherapy (n = 47)	p-value
Seizure-Free	78%	49%	0.002
Breakthrough Seizures	22%	51%	0.001
Status Epilepticus	1%	4%	0.05

Seizure control was significantly better in the monotherapy group, highlighting the importance of simplified treatment regimens during pregnancy. Polytherapy regimens, though sometimes necessary for refractory epilepsy, were associated with a higher incidence of breakthrough seizures and status epilepticus.

Congenital anomalies were more frequent in the polytherapy group (19%) compared to the monotherapy group (6%). Low birth weight and preterm births were also more common in pregnancies exposed to sodium valproate.

Table No. 3: Fetal Outcomes by AED Type

Outcome	Lamotrigine (n = 50)	Levetiracetam (n = 45)	Sodium Valproate (n = 40)	p-value
Congenital Anomalies (%)	4	7	18	0.01
Low Birth Weight (%)	6	8	22	0.001
Preterm Birth (%)	10	12	25	0.002

Sodium valproate was associated with the highest rates of adverse fetal outcomes, including congenital anomalies and low birth weight. Lamotrigine and levetiracetam, in contrast, demonstrated a safer profile, with lower incidences of complications. Drug adherence rates were higher in the monotherapy group (85%) compared to the polytherapy group (62%). Regular monitoring of AED levels was associated with better seizure control and fewer adverse outcomes.

Table No. 4: Drug Adherence and Monitoring

Parameter	Monotherapy (%)	Polytherapy (%)	p-value
Drug Adherence	85	62	0.03
Therapeutic Drug Levels	92	78	0.04

Higher adherence rates and therapeutic monitoring in the monotherapy group highlight the importance of patient education and frequent follow-up visits to optimize maternal and fetal outcomes. Dose adjustments were required in 60% of patients due to altered pharmacokinetics during pregnancy. Lamotrigine required the most frequent adjustments (72%), followed by levetiracetam (65%) and sodium valproate (45%).

Table No. 5: AED Dose Adjustments During Pregnancy

AED Type	Dose Adjustments Required (%)
Lamotrigine	72
Levetiracetam	65
Sodium Valproate	45
Polytherapy	58

Lamotrigine exhibited the highest requirement for dose adjustments, reflecting its increased clearance during pregnancy. This underscores the importance of therapeutic drug monitoring (TDM) to ensure adequate seizure control while avoiding toxicity. Perinatal complications such as neonatal intensive care unit (NICU) admissions and low Apgar scores (<7 at 1 minute) were more frequent in pregnancies exposed to sodium valproate and polytherapy regimens.

Table No. 6: Perinatal Complications and Neonatal Outcomes

Outcome	Monotherapy (%)	Polytherapy (%)	Sodium Valproate (%)	p-value
NICU Admissions	5	15	20	0.01
Low Apgar Scores (<7)	8	18	22	0.002
Neonatal Mortality	0	2	4	0.05

DISCUSSION

Maintaining effective seizure control during pregnancy is crucial to minimize maternal complications and improve overall outcomes. This study found that seizure-free pregnancies were significantly more common in women on monotherapy (78%) compared to those on polytherapy (49%). This supports the findings from other studies, who emphasized that monotherapy regimens are preferred due to their lower risk of maternal and fetal complications while maintaining adequate seizure control[11]. The study explored the maternal and fetal outcomes of women with epilepsy (WWE) during pregnancy, focusing on various treatment regimens, including monotherapy and polytherapy, and the impact of specific antiepileptic drugs (AEDs) on pregnancy outcomes. The results highlight several key trends that underline the importance of treatment optimization and monitoring during pregnancy for WWE[12]. The data from Table 1 show that most patients had focal epilepsy (62%), with a significant proportion of women (65%) being treated with monotherapy. Seizure control was notably better in the monotherapy group, with 78% of patients in this group remaining seizure-free throughout their pregnancies compared to just 49% in the polytherapy group. This difference is statistically significant ($p = 0.002$) and suggests that monotherapy is associated with improved seizure control during pregnancy, which is crucial for both maternal and fetal health[13]. Additionally, breakthrough seizures occurred less frequently in the monotherapy group, with only 22% of patients experiencing seizures, compared to 51% in the polytherapy group ($p = 0.001$). These findings align with previous literature that suggests simpler AED regimens during pregnancy result in better seizure control and fewer complications[14].

However, for women requiring polytherapy, the risk of breakthrough seizures and status epilepticus was higher, as demonstrated by a higher incidence of status epilepticus (4% in polytherapy vs. 1% in monotherapy). These findings emphasize the need for careful management of patients with refractory epilepsy, who may require multiple AEDs but face greater risks. The

study also assessed fetal outcomes based on the type of AED used (Table 3). Sodium valproate, which is commonly prescribed for generalized epilepsy, was associated with the highest rates of adverse fetal outcomes, including congenital anomalies (18%), low birth weight (22%), and preterm births (25%). These results are consistent with previous studies linking sodium valproate exposure to a higher risk of congenital defects and adverse neonatal outcomes. Lamotrigine and levetiracetam were associated with a safer fetal profile, with lower rates of congenital anomalies (4% and 7%, respectively) and preterm birth (10% and 12%, respectively). These findings suggest that lamotrigine and levetiracetam may be safer alternatives to sodium valproate for managing epilepsy in pregnancy, aligning with current guidelines that recommend these AEDs as first-line treatment for women of childbearing age[15]. Drug adherence and therapeutic drug monitoring (TDM) were significantly better in the monotherapy group, with 85% adherence compared to 62% in the polytherapy group ($p = 0.03$)[16]. The need for dose adjustments during pregnancy was more pronounced in the monotherapy group, especially for lamotrigine, which required the most frequent adjustments (72%) due to its increased clearance during pregnancy. This highlights the importance of TDM to ensure adequate seizure control while avoiding toxicity. Levetiracetam and sodium valproate also required dose adjustments, though less frequently than lamotrigine (65% and 45%, respectively). These adjustments further emphasize the need for careful monitoring and individualized treatment plans to ensure optimal seizure control and minimize adverse effects on both the mother and fetus[17]. The perinatal outcomes, as shown in Table 6, indicate that polytherapy and sodium valproate exposure were linked to higher rates of NICU admissions, low Apgar scores, and neonatal mortality. In particular, the polytherapy group had a higher incidence of NICU admissions (15% vs. 5% in the monotherapy group) and low Apgar scores (18% vs. 8% in the monotherapy group)[18]. Sodium valproate exposure was also associated with higher rates of these complications, further supporting the notion that sodium valproate may be a risk factor for poor neonatal outcomes. These findings highlight the importance of careful AED selection and the potential benefits of monotherapy in reducing the risk of perinatal complications.

CONCLUSION

The choice of AEDs significantly impacts maternal seizure control and fetal outcomes. Monotherapy regimens, particularly lamotrigine and levetiracetam, were associated with better maternal seizure control and fewer adverse fetal outcomes compared to polytherapy regimens.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Ayesha Saleem, Rutaba Qadri
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