MANAGEMENT OF EPILEPSY DURING PREGNANCY: CLINICAL EFFICACY AND SAFETY OF ANTIEPILEPTIC THERAPY

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ABSTRACT: *Epilepsy is one of the most prevalent chronic neurological disorders among women of reproductive age, affecting approximately 1% of the global population. The concurrent management of epilepsy during pregnancy presents a significant clinical challenge, as both uncontrolled seizures and antiepileptic drug (AED) exposure may adversely affect maternal and fetal outcomes. This retrospective observational study aimed to evaluate the clinical efficacy and safety of antiepileptic therapy in pregnant women with epilepsy.*

A total of 15 pregnant women diagnosed with epilepsy were monitored between 2024 and 2026 at the Department of Neurology, Tashkent State Medical University. Clinical data encompassing seizure frequency, epilepsy type, prescribed AEDs, adverse drug reactions, and pregnancy outcomes were systematically collected and analyzed using descriptive statistical methods.

The mean patient age was 27.4 ± 4.2 years. Levetiracetam (n=6; 40%) and Lamotrigine (n=4; 27%) were the most frequently prescribed AEDs, consistent with their recognized favorable teratogenic safety profiles. Seizure frequency was reduced by more than 50% in 11 of 15 patients (73.3%). Mild adverse effects — including dizziness, somnolence, nausea, and mild skin rash — were observed in 3 patients (20%) and did not necessitate discontinuation

of therapy. Combination therapy was employed in refractory cases with acceptable clinical tolerability. No severe congenital malformations or serious obstetric complications were documented during the observation period.

The findings of this study underscore the critical importance of individualized, evidence-based AED selection and continuous neurological monitoring throughout pregnancy. Appropriate therapeutic strategies, multidisciplinary collaboration, and regular follow-up significantly contribute to optimizing both maternal and fetal outcomes in women with epilepsy.

Keywords: *Epilepsy; Pregnancy; Antiepileptic drugs (AEDs); Levetiracetam; Lamotrigine; Valproate; Seizure control; Teratogenicity; Maternal outcomes; Fetal safety.*

1. INTRODUCTION

1.1. Background and Relevance of the Topic

Epilepsy is a chronic neurological disorder characterized by recurrent, unprovoked seizures arising from abnormal and excessive electrical discharges in the brain. It is one of the most common serious neurological conditions worldwide, affecting approximately 50 million people globally, with a prevalence of approximately 1% in the general population (WHO, 2023). Among these, a substantial proportion consists of women of childbearing age, making epilepsy during pregnancy a clinically critical and increasingly relevant public health concern.

In Uzbekistan, neurological disorders — including epilepsy — represent a significant burden on the healthcare system. Growing rates of diagnosis among women of reproductive age necessitate evidence-based clinical protocols that balance therapeutic efficacy with fetal safety. Despite advances in pharmacological treatment over recent decades, the management of epilepsy during pregnancy remains one of the most complex challenges in clinical neurology and obstetrics.

The dual risk posed by this condition — uncontrolled seizures on one hand, and the potential teratogenic effects of antiepileptic drugs (AEDs) on the other — demands a highly individualized, multidisciplinary therapeutic approach. Generalized tonic-clonic seizures during pregnancy are associated with a range of adverse outcomes, including maternal trauma, fetal hypoxia, placental abruption, preterm labor, and, in severe cases, fetal or maternal death. Simultaneously, exposure to certain AEDs during the first trimester of pregnancy has been associated with an elevated risk of major congenital malformations, neurodevelopmental impairment, and intrauterine growth restriction.

These considerations place the clinician in a delicate position: seizure control must be maintained to protect both the mother and the developing fetus, while the selection of AEDs must account for their potential teratogenic profiles. In recent years, significant progress has been made in identifying safer pharmacological options. Levetiracetam and Lamotrigine have emerged as preferred first-line agents due to their favorable safety records in pregnancy, whereas Valproate — despite its high efficacy — is increasingly restricted due to its well-documented association with neural tube defects and adverse neurodevelopmental outcomes.

1.2. Review of Existing Literature

International studies have extensively examined the relationship between AED use and pregnancy outcomes. A landmark multicenter study by the EURAP International Registry (2006–2020) documented major congenital malformation rates across various AEDs, consistently identifying Valproate as the highest-risk agent (malformation rate: 10.3%) compared to Levetiracetam (2.8%) and Lamotrigine (2.9%). These findings have been replicated across multiple independent cohort studies and have formed the basis for updated clinical guidelines issued by the International League Against Epilepsy (ILAE, 2019) and the European Academy of Neurology (EAN, 2022).

Liu et al. (2024) demonstrated the high efficacy of Levetiracetam in pediatric and adult epilepsy populations, with a favorable adverse effect profile and no documented increase in congenital malformation rates. Similarly, Zhai et al. (2024) reported that novel AEDs, including Lamotrigine and Levetiracetam, offer significant advantages over older drugs in terms of both tolerability and fetal safety. Tu et al. (2025) conducted a comprehensive systematic review of lamotrigine-associated adverse events, confirming that mild skin reactions are the most commonly reported side effect, rarely necessitating drug withdrawal.

Despite this growing body of evidence, the majority of high-quality studies originate from Western or East Asian clinical settings. Data from Central Asian populations — including Uzbekistan — remain scarce, highlighting a significant gap in the regional clinical literature. This study addresses that gap by providing preliminary observational data from a domestic neurological department, contributing to the evidence base for locally applicable treatment protocols.

1.3. Research Gap and Justification

While global guidelines provide comprehensive recommendations for AED use during pregnancy, their direct applicability to the Central Asian clinical context may be limited due to differences in population genetics, healthcare infrastructure, drug availability, and prescribing practices. The absence of local observational data constrains the ability of clinicians in Uzbekistan to adapt international recommendations to their specific patient populations.

This study addresses this gap through a structured retrospective analysis of 15 pregnant women with epilepsy managed at a tertiary neurological center in Tashkent. Although the sample is limited in size — a recognized constraint of the study — the findings offer a clinically meaningful preliminary

perspective on local prescribing practices, treatment efficacy, and short-term maternal and fetal safety outcomes.

1.4. Aim and Objectives

The aim of this study was to evaluate the clinical efficacy and safety of antiepileptic therapy in pregnant women with epilepsy.

The specific objectives were as follows:

- To describe the demographic and clinical characteristics of pregnant women with epilepsy in the study cohort;
- To analyze the pattern of AED prescribing, including drug type and frequency of use;
- To assess the efficacy of antiepileptic treatment as measured by seizure frequency reduction;
- To evaluate the safety of prescribed AEDs, including the nature and frequency of adverse drug reactions;
- To document pregnancy outcomes within the observation period.

2. MATERIALS AND METHODS

2.1. Study Design

A retrospective observational study was conducted at the Department of Neurology and Medical Psychology, Tashkent State Medical University, covering the period from January 2024 to March 2026. The retrospective design was selected given the ethical constraints of conducting prospective experimental interventions in a pregnant population, and to allow for the systematic review of existing clinical documentation.

2.2. Study Population

The study included 15 pregnant women who had been diagnosed with epilepsy and received antiepileptic pharmacotherapy during pregnancy. All patients were managed within the outpatient and inpatient services of the neurology department. Given the small and fixed sample size, all eligible cases

identified during the study period were included; no random sampling was applied.

2.3. Inclusion and Exclusion Criteria

Patients were included in the study if they met all of the following criteria:

- Confirmed diagnosis of epilepsy established prior to or during pregnancy;
- Age between 18 and 40 years;
- Actively receiving antiepileptic drug therapy at the time of monitoring;
- Availability of complete and retrievable clinical records.

Patients were excluded if any of the following applied:

- Presence of severe concurrent systemic diseases (e.g., renal failure, hepatic insufficiency, autoimmune disorders);
- Incomplete or inaccessible medical documentation;
- Documented non-compliance with prescribed therapeutic regimens;
- Diagnosis of symptomatic epilepsy attributable to a structural or metabolic cause requiring separate management.

2.4. Data Collection

Clinical data were extracted from patient medical records using a standardized data collection form. The following variables were recorded for each patient: age; gestational week at initial assessment; epilepsy type and duration; seizure type and pre-treatment frequency; prescribed antiepileptic drugs, including dose and duration; adverse drug reactions (nature, severity, and management); and pregnancy outcomes (including delivery mode, gestational age at delivery, and neonatal condition).

2.5. Assessment of Efficacy and Safety

Treatment efficacy was defined as a reduction in seizure frequency of 50% or more compared to the baseline period prior to the initiation or optimization of therapy during pregnancy. Patients achieving this threshold were classified as treatment responders. Seizure remission was defined as complete absence of seizures for a minimum of three consecutive months during the observation period.

Safety was assessed through systematic documentation of adverse drug reactions. Adverse effects were classified according to severity as mild (requiring no change in therapy), moderate (requiring dose adjustment), or severe (necessitating drug discontinuation). Fetal safety was evaluated on the basis of neonatal examination findings, and the presence or absence of congenital malformations was recorded.

2.6. Statistical Analysis

All collected data were entered into a structured database and analyzed using descriptive statistical methods. Continuous variables are presented as mean ± standard deviation (SD). Categorical variables are expressed as absolute frequencies and percentages. Given the small sample size (n = 15), inferential statistical testing was not performed, and no claims of statistical significance are made. The findings are intended to be hypothesis-generating and descriptive in nature, providing preliminary clinical observations for a population that has not previously been characterized in the local literature.

2.7. Ethical Considerations

The study was conducted in full accordance with the ethical principles of the Declaration of Helsinki (2013 revision). Patient data were anonymized prior to analysis, and no personally identifiable information is reported. As a retrospective study involving secondary data only, formal informed consent from individual patients was not required; however, institutional approval for data access was obtained from the relevant departmental authority.

3. RESULTS

3.1. Demographic and Clinical Characteristics

A total of 15 pregnant women with a confirmed diagnosis of epilepsy were included in the study. The mean age of the study population was 27.4 ± 4.2 years (range: 19–36 years). The mean duration of epilepsy prior to the current pregnancy was 5.8 ± 3.1 years. The majority of patients (n = 10; 66.7%) had focal epilepsy, while 5 patients (33.3%) had generalized epilepsy. All patients were in the second or third trimester at the time of initial assessment in the neurology department.

Table 1. Demographic and Clinical Characteristics of Study Patients (n = 15)

Parameter	Value
Mean age (years)	27.4 ± 4.2
Age range (years)	19 – 36
Mean epilepsy duration (years)	5.8 ± 3.1
Focal epilepsy, n (%)	10 (66.7%)
Generalized epilepsy, n (%)	5 (33.3%)
Patients on monotherapy, n (%)	12 (80.0%)
Patients on combination therapy, n (%)	3 (20.0%)

3.2. Antiepileptic Drug Prescribing Patterns

Levetiracetam was the most frequently prescribed AED, used in 6 patients (40.0%), followed by Lamotrigine in 4 patients (26.7%), Valproate in 3 patients (20.0%), and Carbamazepine in 2 patients (13.3%). Monotherapy

was the primary treatment approach in 12 patients (80.0%), while combination therapy was employed in 3 patients (20.0%) who had been classified as having refractory epilepsy.

Table 2. Distribution of Antiepileptic Drug Use and Associated Adverse Effects

Antiepileptic Drug	No. of Patients	Proportion (%)	Main Adverse Effects Reported
Levetiracetam	6	40.0%	Dizziness, somnolence
Lamotrigine	4	26.7%	Mild skin rash, headache
Valproate	3	20.0%	Weight gain, nausea
Carbamazepine	2	13.3%	Somnolence, dizziness

3.3. Treatment Efficacy

Treatment efficacy was assessed based on reduction in seizure frequency relative to baseline. A clinically significant reduction in seizure frequency of 50% or more was observed in 11 of 15 patients (73.3%), fulfilling the study's predefined criterion for treatment response. Complete seizure remission — defined as absence of seizures for a minimum of three consecutive months — was documented in 5 patients (33.3%), all of whom were receiving monotherapy with either Levetiracetam or Lamotrigine.

In the remaining 4 patients (26.7%), seizure frequency decreased by less than 50% from baseline. Of these, 3 were receiving combination therapy for refractory epilepsy, and 1 was on Valproate monotherapy. No patient experienced a worsening of seizure frequency during the observation period.

Table 3. Summary of Treatment Efficacy Outcomes

Efficacy Outcome	No. of Patients	Proportion (%)
Seizure frequency reduction ≥ 50%	11	73.3%
Complete seizure remission (≥ 3 months)	5	33.3%
Seizure frequency reduction < 50%	4	26.7%
Worsening of seizure frequency	0	0.0%

3.4. Safety Profile and Adverse Drug Reactions

Adverse drug reactions (ADRs) were documented in 3 of 15 patients (20.0%). All reported ADRs were classified as mild in severity and did not require discontinuation or modification of the prescribed antiepileptic regimen. The most commonly reported adverse effects were dizziness and somnolence (n = 2), associated with Levetiracetam and Carbamazepine use, and mild skin rash (n = 1), reported in a patient receiving Lamotrigine. No moderate or severe adverse effects were identified. No hepatotoxicity, hematological abnormalities, or serious hypersensitivity reactions were observed in any patient.

3.5. Pregnancy and Neonatal Outcomes

No major congenital malformations were identified in any of the 15 neonates within the observation period. No cases of stillbirth, neonatal seizures, or clinically significant neonatal complications were documented. Three patients (20.0%) delivered via elective cesarean section, indicated for obstetric rather than neurological reasons. The remaining 12 patients (80.0%) had uncomplicated vaginal deliveries. All neonates were assessed as clinically stable at delivery. Long-term neurodevelopmental follow-up of the neonates was beyond the scope of the present study.

4. DISCUSSION

4.1. Interpretation of Findings

The results of this retrospective observational study demonstrate that individualized antiepileptic pharmacotherapy — guided by teratogenic safety considerations — can achieve meaningful seizure control in pregnant women with epilepsy, without incurring significant short-term maternal or fetal harm. A seizure response rate of 73.3% and a remission rate of 33.3% compare favorably with published data from larger international cohorts, where response rates typically range between 60% and 80% in pregnancy-adapted treatment protocols (Najafi et al., 2025).

The predominant use of Levetiracetam and Lamotrigine in this cohort reflects alignment with current international guidelines, which recommend these agents as first-line pharmacotherapy for epilepsy during pregnancy due to their relatively low teratogenic risk compared to older-generation AEDs such as Valproate and Carbamazepine (ILAE, 2019; EAN, 2022). The complete absence of major congenital malformations in this cohort, although partly attributable to the small sample size, is consistent with the established safety profiles of the predominantly used drugs.

4.2. Comparison with Published Literature

The findings of this study are largely consistent with those reported in recent international literature. Liu et al. (2024) documented high seizure control rates with Levetiracetam across multiple epilepsy subtypes, with a tolerable adverse effect profile and no significant teratogenic risk. Similarly, Tu et al. (2025) confirmed that Lamotrigine is associated with predominantly mild and self-limiting adverse effects — most commonly skin reactions — which rarely require therapeutic modification. The 20% adverse effect rate observed in the present study aligns with these published figures.

The use of Valproate in 3 patients (20.0%) in this cohort warrants specific attention. Valproate is recognized as the most teratogenic AED in

current clinical use, associated with neural tube defects in 1–2% of exposed pregnancies, cardiac malformations, orofacial clefts, and — critically — dose-dependent impairment of cognitive development and IQ in exposed children (De Bellis et al., 2025). Regulatory authorities in the European Union have imposed severe prescribing restrictions for Valproate in women of childbearing potential. While no adverse fetal outcomes were documented in the Valproate-exposed patients in this cohort — likely due to the small numbers and limited follow-up — the prescribing of Valproate during pregnancy should be subject to rigorous individual risk-benefit analysis and, where possible, transition to safer alternatives should be pursued prior to conception.

Combination therapy was employed in 3 patients with refractory epilepsy, consistent with the findings of Yan et al. (2025), who demonstrated that carefully selected combination regimens can provide improved seizure control following failure of Valproate monotherapy, with acceptable tolerability. Li (2025) further affirmed that rational polytherapy — combining agents with complementary mechanisms of action — can offer clinically meaningful benefits in treatment-resistant cases, provided that pharmacokinetic interactions are carefully monitored.

4.3. Clinical Implications

The findings of this study carry several important clinical implications for the management of epilepsy in pregnant women within the Uzbek healthcare context. First, they support the adoption and reinforcement of international evidence-based prescribing guidelines — specifically the preferential use of Levetiracetam and Lamotrigine — in local clinical practice. Second, they highlight the need for pre-conception counseling for women with epilepsy, enabling planned transitions away from high-risk agents such as Valproate before pregnancy is established. Third, they underscore the value of a multidisciplinary approach involving neurologists, obstetricians, and clinical pharmacists in the coordinated management of this complex patient population.

Regular seizure monitoring, plasma drug level surveillance, and structured obstetric follow-up are essential components of optimal care. The development of standardized institutional protocols for the management of epilepsy in pregnancy — informed by both international evidence and local clinical data — is a priority that future research in this setting should address.

4.4. Limitations of the Study

Several limitations of this study must be acknowledged. The most significant limitation is the small sample size of 15 patients, which substantially constrains the statistical power of the study and the generalizability of the findings. No comparative or control group was included, preventing comparison between treatment-exposed and unexposed pregnant women. The retrospective design introduces the potential for selection bias and incomplete data ascertainment. Furthermore, the observation period did not extend beyond delivery, and long-term neonatal neurodevelopmental outcomes — which represent one of the most clinically important endpoints in this population — were not assessed. Drug plasma concentrations were not systematically measured, limiting the precision of exposure characterization.

These limitations are recognized by the authors and are acknowledged transparently. The study is intended to serve as a hypothesis-generating preliminary investigation rather than a definitive clinical trial. Future prospective studies with larger sample sizes, standardized exposure assessment, and long-term follow-up are strongly encouraged.

5. CONCLUSION AND RECOMMENDATIONS

5.1. Conclusion

This retrospective observational study provides preliminary evidence that individualized antiepileptic pharmacotherapy, guided by established principles of teratogenic safety and evidence-based drug selection, can

effectively control seizures in pregnant women with epilepsy while maintaining an acceptable short-term maternal and fetal safety profile.

Levetiracetam and Lamotrigine demonstrated favorable efficacy and tolerability in this cohort, with a treatment response rate of 73.3% and no documented cases of major congenital malformations or severe obstetric complications. Adverse drug reactions were observed in 20% of patients, all of mild severity and not requiring discontinuation of therapy.

These findings are consistent with current international clinical guidelines and support the integration of evidence-based prescribing protocols into local neurological and obstetric practice in Uzbekistan. The use of Valproate during pregnancy remains a concern requiring individualized clinical judgement and, where possible, proactive transition to safer pharmacological alternatives.

5.2. Practical Recommendations

Based on the findings of this study, the following practical recommendations are proposed:

- Levetiracetam and Lamotrigine should be considered as preferred first-line antiepileptic agents for women of childbearing age and for pregnant women with epilepsy in the Uzbek clinical setting.
- Pre-conception neurological counseling should be routinely offered to all women with epilepsy of reproductive age, with proactive review and, where clinically feasible, modification of high-risk pharmacotherapy prior to planned pregnancy.
- The use of Valproate during pregnancy should be subject to strict individual benefit-risk assessment; its use should be reserved for cases where no effective alternative exists and should be accompanied by enhanced monitoring.

- Multidisciplinary collaboration between neurologists, obstetricians, and pharmacists is essential throughout the management of epilepsy in pregnancy.
- Regular clinical monitoring, including seizure frequency assessment and clinical review, should be maintained throughout all trimesters of pregnancy.
- Future prospective studies with larger patient cohorts and long-term neonatal neurodevelopmental follow-up are strongly recommended to build upon the preliminary findings of the present study.

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