

RESEARCH ARTICLE

Pregnancy with epilepsy and antiepileptic drug therapy on fetomaternal outcome

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ABSTRACT

Background: Pregnancy women with epilepsy may have higher chances of obstetric complications, aggregative seizures, major congenital malformations, and abnormal deliveries. Monotherapy or polytherapy of anti-epileptic drugs are usually associated with adverse outcomes in pregnant women with epilepsy. **Aim and Objectives:** The aim of the study was to evaluate the effect of epilepsy and antiepileptic drug (AED) therapy on the fetomaternal outcome in pregnant women. **Material and Methods:** A total of 46 pregnant women with epileptic seizures between 18 and 35 years with mean age of 26.46 years were included in the study. The demographic, clinical, and obstetrical data were collected from the medical records. The AED monotherapy and polytherapy with drug dosage details were noted. The details of mode of delivery, outcome of seizures in post-natal period and fetal outcome were gathered. **Results:** About 65.21% cases were under AED polytherapy and 34.78% cases were under AED monotherapy. Majority cases had carbamazepine (CBZ) and sodium valproate mono and polytherapy. Majority had normal vaginal delivery (65.11%). Single or in combination use of sodium valproate, CBZ, and phenytoin are associated with major congenital malformations (9%). Postpartum hemorrhage was observed in 6.52% cases and postpartum seizure occurrence was observed in 8.69% cases. **Conclusion:** A well planned pregnancy, continuous monitoring for congenital malformations and fetal growth restriction is necessary in pregnant women under AED therapy for better maternal and fetal outcome.


KEY WORDS: Pregnancy; Anti-epileptic Drugs; Major Congenital Malformations

INTRODUCTION

The epilepsy and its management in pregnant women are difficult as antiepileptic drugs (AEDs) and seizures have noxious impact on maternal and fetal health.^[1,2] Several studies reported that seizures in pregnancy are associated with preterm deliveries, still births, postpartum bleeding, higher incidence of cesarean section, miscarriage, and congenital

malformations.^[3] The higher incidences of seizures during pregnancy are associated with preexisting uncontrolled seizures and pregnancy induced complications.^[4] The conventional AEDs such as sodium valproate and phenytoin are associated with teratogenic effects. In recent days, new AEDs such as lamotrigine and levetiracetam have less teratogenic effect than conventional AEDs.^[5,6] The pregnant woman medicated with sodium valproate and carbamazepine (CBZ) is associated with adverse fetal outcomes such as major congenital malformations, fetal growth retardations, skeletal abnormalities, microcephaly, cardiac effects, and spina bifida.^[7]

It is difficult to obtain prompt evidence on the effects of epilepsy seizures in the pregnant women and AED therapy on the developing fetus is difficult. With the minimal

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availability of literature in the local context, the present study was designed to evaluate the effect of epilepsy and AED therapy on the fetomaternal outcome in pregnant women.

MATERIALS AND METHODS

The present study was conceptualized and conducted in the Department of Anatomy, MNR Medical College and Hospital, Sangareddy. A total of 46 female participants between 18 and 35 years, clinically diagnosed with generalized tonic clonic seizures (GTCS), myoclonic seizures, and absence seizures based on criteria of the commission and terminology of the international league against epilepsy by qualified neurologist were recruited. Informed consent was obtained from participants or parent/guardians before the study and study protocol was approved by institutional ethics committee (No. IEC: MNRMC/EC/638). The participants with evidence of structural, metabolic, and other chronic neurological disorders and not willing to participate in the study were excluded from the study.

The structured pro forma was used to gather the demographic data (age, marital status, economic status, educational status, occupation, and residence), clinical data (type of seizure, onset of seizures, frequency and duration of seizure, and Electroencephalography), and obstetrical data (gravida, gestational age, and details of labor) of the patients from medical records. The AED monotherapy and polytherapy with drug dosage details was collected. The details of mode of delivery, outcome of seizures in postnatal period, and fetal outcome were gathered.

Descriptive statistics was used to identify the frequency and percentage of demographic, clinical and obstetric data. Statistical analysis was performed using Statistical Package for the Social Sciences 16.0.

RESULTS

The mean age of study participants was 26.46 years [Table 1]. Majority cases had onset of seizures since childhood with idiopathic cause. GTCS (71.73%) were the most common seizure type, followed by myoclonic seizures (19.56%), absence seizure (4.34%), and complex partial seizures (4.34%) [Table 2]. Details of AED therapy are summarized in Table 3. The folic acid intake was seen in 100% of cases. Anemia (47.82%) was most common pregnancy associated complication, followed by pregnancy induced hypertension (8.7%), diabetes mellitus (DM) (2.18%), and 41.3% cases did not show any associated complications. [Table 4]. Normal birth weight was observed in 82.60% cases and low birth weight was seen in 17.40% cases. Congenital malformation was seen in 9% cases. Fetal outcome is depicted in Figure 1. Association of fetal outcome with pregnancy complications, seizure type and AED therapy is summarized in Table 5.

Table 1: Details of demographic data of study participants

Demographic parameter	Total no of cases (n=46)	
	Frequency	Percentage
Age (In years)	26.46±8.62	
Marital status		
Married and united	45	97.82
Divorced	01	2.18
Economic status		
Upper class	03	6.52
Middle class	31	67.39
Lower class	12	26.08
Educational status		
Secondary education	24	52.17
Intermediate	08	17.39
Graduation and above	14	30.43
Occupation		
Housewife	44	95.65
Working	02	4.34

Table 2: Seizure history among study participants

Parameter	Frequency	Percentage
Onset of seizure		
Since childhood	24	52.17
At puberty	18	39.14
During pregnancy	04	8.69
Cause of seizures		
Acquired	08	17.3
Idiopathic	38	82.60
Type of seizures		
GTCS	33	71.73
Myoclonic	09	19.56
Absence	02	4.34
Complex partial	02	4.34

GTCS: Generalized tonic-clonic seizures

DISCUSSION

Seizures during pregnancy can increase the risk of developmental delay. GTCS or series of similar seizure types may leads to the occurrence of stillbirths. Congenital anomalies and congenital malformations of fetus have been associated with intrauterine exposure to AEDs.^[8] The present study was designed to evaluate the fetomaternal outcome in women with pregnancy. This study consists of 46 pregnant women with epileptic seizures between 18 and 35 years with mean age of 26.46 years. The onset of seizure was since childhood in 52.17%, at puberty in 39.14%, and developed during pregnancy in 8.69% cases. In majority cases cause of seizures was unknown. GTCS (71.73%) were the commonest seizure type, followed by myoclonic seizures

Table 3: Details of AED therapy

Drug therapy	Frequency	Percentage
AED monotherapy (n=16)		
CBZ	04	8.69
Sodium Valproate (SV-200 mg)	02	4.34
Sodium Valproate (SV-400 mg)	03	6.5
Levetiracetam	02	4.34
Lamotrigine	01	2.17
Phenytoin	04	8.69
AED polytherapy (n=30)		
SV-200mg+CBZ	16	34.78
Lamotrigine+CBZ	04	8.69
Phenytoin+CBZ	02	4.34
Levetiracetam+CBZ+SV	02	4.34
Phenytoin+CBZ+SV	06	13.0

CBZ: Carbamazepine, AED: Antiepileptic drug

Table 4: Obstetrical data and pregnancy outcome in study participants

Clinical data	Frequency	Percentage
Frequency of seizures during pregnancy		
Increased	13	28.2
Decreased	02	4.34
Remains same	31	67.39
Details of delivery		
Abortions	03	6.5
Pre-term	03	6.5
Full-term	40	86.95
Mode of delivery (n=43)		
Normal	28	65.11
LSCS	13	30.23
Forceps	02	4.6
Postpartum complications		
Hemorrhage	03	6.52
Seizures	04	8.69

LSCS: Lower segment Cesarean section

(19.56%), absence seizure (4.34%), and complex partial seizures (4.34%) [Table 2]. In this study, 65.21% cases were under AED polytherapy and 34.78% cases were under AED monotherapy. Sodium valproate 200 mg with CBZ was the most common drug regimen prescribed in 34.78% cases [Table 3]. Anemia (47.82%) was the most common pregnancy associated complication, followed by pregnancy induced hypertension (8.7%), DM (2.18%), and 41.3% cases did not show any associated complications. The frequency of seizures was increased in 28.2% cases and remains same in 67.39% cases. Abortions and preterm deliveries were seen in 6.5% cases commonly, and full-term deliveries were seen in 86.95% cases. Majority cases had normal vaginal delivery (65.11%). Postpartum hemorrhage was observed in 6.52% cases and postpartum seizure occurrence was

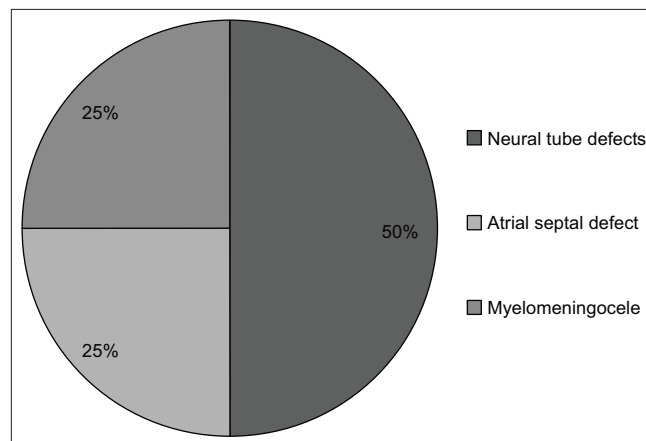


Figure 1: Fetal outcome with congenital malformation

observed in 8.69% cases [Table 4]. Normal birth weight was observed in 82.60% cases and low birth weight was seen in 17.40% cases. Congenital malformation was seen in four cases. In this study, three pregnant women with GTCS and one with complex partial seizures gave birth to congenitally malformed children [Table 5].

A study by Mawer *et al.* noticed increased obstetric complications in pregnancy women during AED therapy. Majority cases had normal vaginal delivery with minimal dominant normal birth weight infants. The higher prevalence of major congenital malformations was associated with sodium valproate (11.3%), followed by lamotrigine (5.4%) and CBZ (3.0%).^[9] The present study CBZ was associated more with the congenital malformations. Kilic *et al.* found no overall effect of AED exposure on gestational age and preterm birth in pregnant woman with epilepsy.^[10] Prakash *et al.* on pregnant women under AED lamotrigine therapy noticed maternal complication such as gestational diabetes (two cases), gestational hypertension and psychiatric complications. One infant born with tracheo-esophageal fistula as major congenital malformations associated with AED therapy.^[11] Pennell stated that sodium valproate has highest degree of risk for major congenital malformations than CBZ, phenytoin, and lamotrigine. AED polytherapy has higher chances of contributing major congenital malformations than AED monotherapy.^[12] A study by Li *et al.* reported abnormal situation such as fetal distress (13.6%), induced abortion (4.5%), mild harelip (4.5%), and trisomy-21 syndrome (4.5%) in epileptic women under AED therapy.^[13] A study by Elvedi-Gašparović *et al.* noticed higher rate of preterm labor in polytherapy (30%) than AED monotherapy (16.6%). Gestational hypertension and seizure during pregnancy were higher in polytherapy group. The major fetal malformations were highly associated with AED monotherapy (3.7%). Two neural tube defects were associated with sodium valproate and one congenital diaphragmatic hernia was associated with CBZ.^[14] A study by Jeon *et al.*,^[15] on pregnant women with epilepsy noticed that 56.25% were under AED monotherapy and 25% were under AED polytherapy. Lamotrigine (29.8%) was the common prescribed AED. The study concluded that

Table 5: Association of fetal outcome with pregnancy complications, seizure type and AED therapy

Fetal outcome	Present		Absent	
	Frequency	Percentage	Frequency	Percentage
Pregnancy complications				
Anemia	–	–	22	47.82
Hypertension	–	–	04	8.69
DM	01	2.17	–	–
No complication	03	6.52	16	34.78
Seizure type				
GTCS	03	6.52	30	65.21
Myoclonic	–	–	09	19.56
Absence	–	–	02	4.34
complex partial	1	2.17	01	2.17
AED therapy				
Monotherapy	02	4.34	14	30.44
Polytherapy	02	4.34	28	60.86

DM: Diabetes mellitus, AED: Antiepileptic drug, GTCS: Generalized tonic-clonic seizures

AED therapy and frequency of seizures are significantly correlated with delivery and fetal outcome.^[16] Melikova *et al.* stated that epilepsy in pregnancy was a significant risk factor for the lower segment cesarean section, preterm birth, and fetal hypoxia.^[16]

In this study, congenital malformation was seen in four cases. In this study, three pregnant women with GTCS and one with complex partial seizures. The prevalence of major congenital malformations was associated with sodium valproate (one case) and CBZ (one case), and in polytherapy with CBZ and lamotrigine (two cases). Among four malformations, two had neural tube defects, one had atrial septal defect, and one had myelomeningocele. The present study was limited to few participants with limited seizure types. Extensive evaluation is require to assess the more AEDs and their effect on pregnancy women with epilepsy.

The pregnancy induced AED exposure affects the fetal growth which is associated with chronic or short term health complication in the affected children. In this study, 65.21% cases were under AED polytherapy and 34.78% cases were under AED monotherapy. Poor seizure control was seen in few cases and majority had normal vaginal delivery. Single or in combination use of sodium valproate and CBZ is associated with incidence of congenital malformations. A well planned pregnancy, continuous monitoring for congenital malformations and fetal growth restriction is necessary in pregnant women under AED therapy for better maternal and fetal outcome.

CONCLUSION

A well planned pregnancy, continuous monitoring for congenital malformations and fetal growth restriction is

necessary in pregnant women under AED therapy for better maternal and fetal outcome.

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