Section: Obstetrics and Gynaecology

Original Research Article

A STUDY OF OBSTETRIC AND PERINATAL OUTCOME IN EPILEPSY COMPLICATING PREGNANCY

Vaseela Banu A[1], Rosalind T[1]

[1]Assistant Professor, Department of Obstetrics and Gynaecology, Tirunelveli Medical College Hospital, Tamilnadu, India

Received : 14/01/2023
Received in revised form : 20/02/2023
Accepted : 05/03/2023

Keywords:
Epilepsy, Neonatal seizures, Obstetric, Perinatal outcome, Pregnancy, Maternal prognosis, Monotherapy.

Corresponding Author:
Dr. Rosalind T,
Email: trosalind@yahoo.co.in

DOI: 10.47009/jamp.2023.5.2.272

Source of Support: Nil,
Conflict of Interest: None declared

Int J Acad Med Pharm
2023; 5 (2); 1286-1292

Abstract

Background: Epilepsy is an extensive disorder that can be primary or secondary to underlying conditions, provoked or unprovoked, childhood or recurrent. A good history taking is essential for proper management and prevention of episodes during pregnancy. The main objectives are to study the percentage of women who have seizures during pregnancy, obstetric outcomes, and perinatal outcomes of women with epilepsy. **Materials and Methods:** This prospective cross-sectional study of obstetric and perinatal outcomes of epilepsy-complicating pregnancy was conducted on 100 pregnant women with epilepsy admitted to TVMCH. Pregnant women with a history of epilepsy or new onset seizures are admitted to the Labor ward for a detailed history, comorbidities, menstrual and marital histories, and a general examination. The fetal outcome is determined based on birth weight, Apgar scores, and associated anomalies. **Result:** The study included 100 women with epilepsy, with generalized tonic-clonic seizures being the most common presentation. Monotherapy was the preferred treatment, with Carbamazepine and Levetiracetam being the most common treatments. 43% had abnormal EEG and radiographical findings, and gestational hypertension was the most commonly associated comorbidity. Cesarean section rates were slightly higher than normal vaginal deliveries, and postpartum hemorrhage was the most common complication. The overall perinatal outcome was good. There is a significant difference in the onset of illness and maternal prognosis between seizures. There is a significant difference in treatment between the 1st and 2nd lines (p=<0.0001). **Conclusion:** Multidisciplinary disease management, including regular follow-up, breastfeeding, and counselling about oral contraceptive pills and intrauterine contraceptive devices, is necessary.

INTRODUCTION

Seizures during any part of life can cause physical and mental upset leading to decreased quality of life. Epilepsy itself is an extensive denomination and not a single disease entity. It presents in various forms, requires different treatments and involves multiple bodily systems. It can be primary or secondary to underlying conditions, provoked or unprovoked, childhood or recurrent.[1] A good history taking regarding the age of occurrence of a seizure, any history of the difficult birth of the mother, the past management done, the number of episodes since the first fit, the number of drugs used to treat, etc., are essential for proper management of the disease and prevent any episodes during pregnancy and for counselling the patient regarding further prospects. Epilepsy is not a contraindication to pregnancy, but pregnant women with epilepsy belong to high risk, and any episode during pregnancy can harm mother and baby. Hence epilepsy should be diagnosed before conception or early pregnancy to prevent complications through proper counselling and safe medications.[2]

Neonatal seizures are due to perinatal hypoxia, intracranial hemorrhage, genetic disorders, metabolic disturbances, fever, CNS infection, trauma, developmental disorders, trauma, substance abuse, cerebrovascular disease, and tumors. Adult seizures are due to trauma, CNS infection, substance abuse, cerebrovascular disease, and tumors. Epilepsy surgery is a newer advance in treatment. Epilepsy is one of the most common neurological conditions in pregnancy, the most familiar headache.[3] About 0.5 to 1% of pregnancy is complicated by seizures.[4] It causes increased maternal and perinatal adverse efforts. It can be due to existing seizure disorders or new onset seizures.

New onset seizures in pregnancy are most common in the second and third trimesters and can occur in

ISSN (O): 2687-5365; ISSN (P): 2753-6556

postpartum. Gestational epilepsy defines women who experience seizures for the first time and remain seizure-free between pregnancies. Risks include increased seizures and congenital fetal malformations due to antiepileptic drug-related teratogenicity.[5] Women with no seizure episodes for at least nine months before conception will likely remain seizure-free during pregnancy.[6]

Anticonvulsant therapy's most important goal is controlling seizures and preventing recurrence. Monotherapy is most commonly preferred though polytherapy is started when seizures are poorly maintained. Poorly controlled seizures increase maternal morbidity and mortality and can lead to SUDEP. Polytherapy increases the risk of congenital malformations. Careful choice of antiepileptic drugs can reduce the need for polytherapy. The main objectives are to study the percentage of women who have seizures during pregnancy, obstetric outcome, and perinatal outcome of women with epilepsy.

MATERIALS AND METHODS

This prospective cross-sectional study of obstetric and perinatal outcomes of epilepsy-complicating pregnancy was conducted in Government Tirunelveli Medical College Hospital from October 2019 to October 2021 for two years.

Ethical committee approval and informed consent were obtained for the study, and 100 pregnant women with epilepsy admitted to TVMCH were included after fulfilling the necessary criteria.

Inclusion Criteria

Pregnant women with a history of epilepsy since childhood, singleton and multiple pregnancies primigravida and multigravida, any seizure, on antiepileptic drugs or not on any antiepileptics, monotherapy or polytherapy were included.

Exclusion Criteria

Nonepileptic seizures, eclamptic seizures, or cerebral venous thrombosis were excluded.

Pregnant women with a history of epilepsy or new onset epilepsy are admitted to the Labor ward. A detailed history is obtained regarding their parity, age, booked or unbooked, history, and history of any associated comorbidities like hypertension, diabetes mellitus, tuberculosis, bronchial asthma, heart disease and previous surgical history. Their menstrual and marital histories are asked. If any is noted, previous obstetric history and comorbidities associated with previous pregnancies are enquired.

The history of seizures is enquired in detail. Age of onset of seizure, number of episodes of seizure and the history of last fit of seizure, seizure-free interval, history of intake of antiepileptics, number of drugs taken, compliance to the AEDs and history of folic acid intake are enquired. History of illicit drug use, head injury, tumors and CNS infections are elicited. To rule out the eclamptic cause of the seizure, a history of headache, vomiting, blurred vision, epigastric pain, facial puffiness, pedal oedema and any decrease in urine output are obtained. Vitals noted are blood pressure, pulse rate, oxygen saturation and respiratory rate.

A complete general examination was done, and the cardiovascular and respiratory systems were examined. An abdominal examination was done, and the uterus size and corresponding gestational age were noted. Per vaginal examination is done in patients with complaints of pain, bleeding and labor. A thorough central nervous system examination is done to determine any neurological deficit. Previous ultrasound records and anomaly scans are noted. Ultrasound abdomen is done on admission to assess gestational age, anomalies and growth restriction, if any. MRI brain and EEG were done in patients with recent history of seizures and new onset seizures.

If the patient goes into labor, she is monitored carefully by regular vitals monitoring, cardiotocography and partogram. Induction of labor was done as and when indicated. Elective cesarean and emergency cesarean section are done in case of dire situations. Maternal prognosis is based on seizures during pregnancy and recurrent seizures. Patients are advised to continue drugs even if labor has commenced to prevent seizures during labor pains.

The fetal outcome is based on birth weight, term or preterm, Apgar scores, and associated anomalies. A thorough examination of the baby by a pediatrician was done. IUGR and low birth weight babies are identified. Babies with low Apgar scores and anomalies are admitted and observed. Postpartum 4th stage monitoring is done in the labor ward. Neurologist opinion obtained regarding the continuation of antiepileptic drugs or any change in dosage of medicines. CT brain or MRI brain is taken if needed. The patient is then discharged and advised to continue antiepileptic medications promptly and adequately at home.

A master chart is prepared with all the vital information collected from the patient. Frequencies, percentages, means and 'p' values were calculated and tabulated.

RESULTS

Most of the 100 women studied come under 20 to 24 (40%). Fifteen elderly pregnant women have been admitted with a seizure disorder, with primiparous women being the most commonly affected. 45% of women presented with GTCS, mostly new onset and based on history given by the witness. 29% did not know their type of seizure, most of which were childhood seizures. Out of 100 women, three experienced status epilepticus. 41% had new onset of seizures during pregnancy, 26% had first seizures in their adult life, and 33% had childhood seizures. Most women with epilepsy had less than five years of seizure disorder [Table 1].

ISSN (O): 2687-5365; ISSN (P): 2753-6556

Table 1: Demographic data of the study

		Frequency
Age group	15-19	6
	20-24	40
	25-29	39
	30-34	13
	35-39	2
Obstetric code	Primi	51
	G2	24
	G3	11
	HOB	4
	Postpartum	10
Seizure	Absence	3
	complex partial seizure	7
	focal seizure	9
	GTCS	45
	Not known	29
	partial	3
	pseudoseizure	1
	Status epilepticus	3
Onset of illness	Adult	26
	Childhood	33
	New onset	41
Duration of illness	0-4	46
	5-9	21
	10-14	25
	15-19	8
No of episodes	0	32
	1	43
	2	15
	3	6
	4	3
	6	1
Period of the last episode	Adult	6
	Antepartum	50
	Childhood	25
	Intrapartum	4
	Postabortal	1
	Postpartum	14
Trimester	1st	11
	2nd	13
	3rd	44
	Nil	32

Women had 1 episode of seizure and were well controlled after starting antiepileptics. Antepartum seizures were most common, with 4 having intrapartum seizures. 14% had seizures in their postpartum period due to drug withdrawal, and 3rd-trimester seizures were predominant. Few studies suggest that 1st-trimester seizures are more common [Table 1].

In 1st line, carbamazepine is the most preferred treatment, followed by levetiracetam. Phenytoin was given to patients with controllable seizures. In 2nd line, the most common add-on drug was Levetiracetam 18% and 66% were on monotherapy. In the 3rd line, most patients did not have 3rd adjuvant drugs at 93% [Table 2].

Table 2: Distribution of 1st line, 2nd line, and 3rd line treatment

Frequency	1st line	2nd line	3rd line
Carbamazepine	34	6	1
Levetiracetam	29	18	1
None	10	66	2
Oxcarbamezepine	2	2	93
Phenytoin	23	7	2
Sodium valproate	2	1	1

Monotherapy was the most preferred treatment for 56% of women with epilepsy, with 43% having abnormal EEG records and 70% having no abnormal radiographical findings. Sclerotic lesions were the most common radiographical finding, followed by Cerebral atrophy. 92% of the women with epilepsy were discharged in good health, with 8% leading to maternal mortality. LSCS rates increased slightly, with 16% lost to follow-up and 9% spontaneous abortion. Postpartum haemorrhage was common, followed by 2 cases with HIE during intrapartum seizures and recovered completely. Most of the babies weighed 2 to 3 kg. 10% of the cases were spontaneous abortions. Most babies had no anomalies due to safer new antiepileptics, resulting in lower birth weight and fewer intrauterine deaths [Table 3].

ISSN (O): 2687-5365; ISSN (P): 2753-6556

Table 3: Treatment, findings, complications, and other parameters of the study.

		Frequency
Treatment	Monotherapy	56
	None	10
	Polytherapy	34
EEG	Abnormal	43
	Normal	57
Radiographical finding	Abnormal	30
	Normal	70
Types of lesions	Atrophy	6
	Hemorrhage	2
	Infarction	3
	None	68
	Sclerosis	13
	SOL	4
	thrombosis	4
Comorbidities	Anaemia	2
	GHTN	16
	Heart disease	4
	Hypothyroid	5
	None	60
	Others*	10
	Twins	3
Maternal prognosis	Death	8
	Good	92
Mode of delivery	Abortion	9
	LSCS	37
	Labour Natural	34
	Nil	16
	Outlet forceps	2
	Vacuum	1
	VBAC	1
Postpartum complication	Nil	93
	PPH	5
	HIE	2
Baby weight	0-1	10
	1-2	17
	2-3	54
	3-4	19
Baby term	Abortion	10
	Preterm	27
	Term	63
AGA/LBW	AGA	62
	LBW	28
Baby outcome	IUD	5
	live	85
Anomaly	Ambiguous genitalia	1
	Cleft lip	3
	Hypoplastic left heart	1
	Neural tube defect	2
	None	93

Primiparous women show predominance in admission with a seizure disorder. However, no significant increase in maternal mortality is seen in primi mothers, followed by a higher birth order. Therefore, there is no significant difference in the onset of illness and maternal prognosis between obstetric codes [Table 4].

Table 4: Comparison of onset of illness and maternal prognosis between obstetric code

Obstetric code	Onset of illness			Maternal prognosis	
	Adult	Childhood	New Onset	Death	Good
G2	8	10	6	1	23
G3	4	1	6	0	11
HOB	1	1	2	1	3
Postpartum	5	0	5	1	9
Primi	8	21	22	5	46
P-value	0.0709			0.511	

New onset seizures were predominantly GTCS seizures at 24%, and focal seizures at 8% closely followed. Childhood seizures were complex partial seizures at 3%. Most childhood seizures were not sufficiently evaluated due to the mother's lack of knowledge of the seizure. GTCS seizures and status epilepticus were associated with poor prognosis. 8% had maternal mortality. Among that, only 2% were related to seizure

ISSN (O): 2687-5365; ISSN (P): 2753-6556

disorder. Rest was due to other obstetric and medical causes. There is a significant difference in the onset of illness and maternal prognosis between seizures [Table 5].

Table 5: Comparison of onset of illness and maternal prognosis between seizure.

Seizure	Onset of illness			Maternal prognosis	
	Adult	Childhood	New Onset	Death	Good
Absence	1	1	1	0	3
Complex partial seizure	0	3	4	1	6
Focal seizure	0	1	8	0	9
GTCS	15	6	24	5	40
Not known	9	20	0	0	29
Partial	0	1	2	0	3
Pseudoseizure	0	0	1	0	1
Status epilepticus	1	1	1	2	1
P-value	<0.0001			0.0084	

Carbamazepine is the most common drug used in mono and polytherapy. Phenytoin is commonly added to polytherapy in uncontrolled seizures, primarily postpartum. The common second-line drug used in polytherapy is levetiracetam at 18%. There is a significant difference in treatment between 1st and 2nd line (p=<0.0001) [Table 6].

Table 6: Comparison of treatment with 1st and 2nd line

	1st line			2nd line		
	Monotherapy	None	Polytherapy	Monotherapy	None	Polytherapy
Carbamazepine	24	0	10	0	0	6
Levetiracetam	20	0	9	0	0	18
None	0	10	0	56	10	0
Oxcarbamezepine/ Phenobarbitone	2	0	0	0	0	2
Phenytoin	9	0	14	0	0	7
Sodium valproate	1	0	1	0	0	1
P-value	<0.0001			<0.0001		

34% were on polytherapy, and there was not much difference in women with new-onset seizures or seizures in adulthood. 15% babies born to women taking polytherapy had low birth weight. It was not significant in this study. There is no significant difference in the onset of illness, prenatal outcomes and anomalous baby between 1st line [Table 7].

Table 7: Comparison of onset of illness, prenatal outcome and anomalous baby between 1st line

		1st line			P-value
		Monotherapy	None	Polytherapy	
Onset of illness	Adult	14	0	12	0.154
	childhood	17	6	10	
	new onset	25	4	12	
	Abortion	5	0	5	
Perinatal outcome	AGA	36	7	19	0.691
	LBW	15	3	10	
Anomalous baby	Nil	9	1	13	0.127
	LBW	1	0	0	
	No	40	9	20	
	Yes	6	0	1	

DISCUSSION

Epilepsy is a common neurological disorder during pregnancy, with an increased risk of morbidity and mortality. Diagnosis and proper drug selection can reduce risks. Our study's mean age of increased prevalence is 20 to 29 years. It is almost in correlation with the study by Thomas et al,[7] the mean maternal age is 26 and ranges from 19 to 38 years. In this study, primiparous women topped the list at 51%, and 15% had higher birth orders. Most of the studies had a higher percentage of multiparous women. There is a decreased risk of complications from epilepsy in a second pregnancy.

In this study, the percentage of women having status epilepticus is 3%. In a study by Beach et al,[8] the incidence is 1 to 2%, comparable to ours. According to Li et al,[9] focal seizures were 31.1% of the study group, whereas our study showed only 7 to 14%, and most seizures are sporadic and not frequent.

In our study, 41% were new-onset seizures, and the incidence is slightly higher than in other studies, ranging from 2 to 10%.[0] Structural and metabolic changes like haemorrhage, thrombosis, space-occupying lesions, hypoglycemia, dyselectrolytemia, and aggravated new-onset seizures.

In the study by Li et al,[9] seizures in the first trimester were 18.2%, in the second trimester,

ISSN (O): 2687-5365; ISSN (P): 2753-6556

45.4% and in the third trimester, 36.4%. The percentage in our study was quite comparable for the third and first trimester at 44% and 11%, whereas it was lower at 13% for the second trimester. As seizures are diagnosed in the first trimester, many studies suggest first-trimester seizures to be more common and can be aggravated by hyperemesis gravidarum.

In our study, monotherapy is 56% compared to polytherapy at 34%. 10% of women did not require antiepileptics. It is comparable to a study by Alsfouk et al,[10] where monotherapy was given at 52% and polytherapy at 29%. The most commonly used antiepileptic was carbamazepine (36.5%), followed by levetiracetam (28.24%).

Almost 30% of women had abnormal electroencephalogram activity and radiographical findings. Our study's most common radiographical finding was sclerosis – mesial temporal sclerosis commonly followed by cerebral atrophy. Women with epilepsy during pregnancy in our study had an increased risk of gestational hypertension as an associated comorbidity at 16%. It is followed by heart disease, anaemia, etc. Borthen et al,[11] studies of seizure in pregnancy also revealed an increased incidence of gestational hypertension and pre-eclampsia.

In our study, maternal mortality was 8%, of which only 2% was due to seizure disorder. The rest were due to other comorbidities in women with epilepsy. It is commonly due to uncontrolled status epilepticus and Sudden unexpected death in pregnancy. It is quite comparable to a study by Macdonald et al,[12] that there is an almost 10-fold increase in maternal mortality in seizure-complicating pregnancies.

Our study showed a slight increase in LSCS at 37% compared to Labor natural at 34%. It is comparable to a study by Razaz et al,[13] there is an increase in LSCS rate and labour induction in seizure-complicating pregnancies. A common postpartum complication in our study is postpartum hemorrhage, mainly due to atonicity. Another side effect is intrapartum seizures causing hypoxic-ischemic encephalopathy. It is supported by a study by Borthen et al,[14] there is an increased risk of postpartum hemorrhage due to an increased risk of uterine atonicity.

Most of the babies in our study weighed between 2 to 3 kg, amongst which almost 2/3rd was the appropriate weight for gestational age, and the rest were low birth weight. In a study by Chen et al,[15] there is an increased risk of small for gestational age babies, preterm labor and low birth weight. It is also attributed to exposure to antiepileptic drugs. In this study, low birth weight constituted about 23%, and most women had healthy babies (52%). Preterm deliveries were 24%, and term babies were 51%. There is 10% of women who underwent spontaneous abortion in this study. Almost 90% of women had live births, and there was 5% of intrauterine death.

A fetal carbamazepine syndrome and fetal hypoplastic left heart have been attributed to the use of phenytoin during early pregnancy. Cleft lip and neural tube defects have been seen in 3 and 2 patients. A study found an increase in new-onset seizures in primiparous women, but it is insignificant. Second, gravida who continue antiepileptics has a positive pregnancy outcome. Most new-onset seizures are treated by monotherapy and polytherapy, with monotherapy being the most preferred mode of treatment. Carbamazepine is the most common antiepileptic to be used, followed by levetiracetam. Phenytoin is added to polytherapy in uncontrolled seizures. In our study, congenital malformation was slightly higher in women on monotherapy. This has been attributed to increased doses of carbamazepine, levetiracetam and usage of phenytoin. It is comparable to the study by Kashif et al.[16] No severe craniofacial limb dysplasias have been reported in our study period.

CONCLUSION

Epilepsy-complicating pregnancy needs to be evaluated and treated early to reduce the recurrence of seizures and complications. Low-weight babies are present, but overall outcomes are good. Safe antiepileptic drugs and folic acid tablets also reduce congenital malformations. Multidisciplinary disease management is necessary for good obstetrics and perinatal outcomes. Regular follow-up with a neurologist postnatally to prevent seizure recurrence and breastfeeding should be encouraged. Counselling should be given about oral contraceptive pills as there is a higher rate of failure due to the intake of antiepileptics drugs. Intrauterine contraceptive devices should be advised in patients who want to defer future pregnancies. Early diagnosis and referral to higher centres with the availability of neurologists and imaging modalities are needed for patients with epilepsy so that proper care can be given and thereby reduce maternal and perinatal morbidity and mortality.

REFERENCES

1. Fisher RS, Acevedo C, Arzimanoglou A, Bogacz A, Cross JH, Elger CE, et al. ILAE official report: a practical clinical definition of epilepsy. Epilepsia 2014; 55:475–82.
2. Hart LA, Sibai BM. Seizures in pregnancy: epilepsy, eclampsia, and stroke. Semin Perinatol 2013; 37:207–24.
3. Banerji D. Progress in Clinical Neurosciences, Volume 26. Delhi, India: Byword Books; 2011.
4. Thangaratinam S, Marlin N, Newton S, Weckesser A, Bagary M, Greenhill L, et al. Antiepileptic drug Monitoring in PREgnancy (EMPiRE): a double-blind, randomised trial on effectiveness and acceptability of monitoring strategies. Health Technol Assess 2018; 22:1–152.
5. Tomson T, Xue H, Battino D. Major congenital malformations in children of women with epilepsy. Seizure 2015; 28:46–50.
6. Harden CL, Meador KJ, Pennell PB, Hauser WA, Gronseth GS, French JA, et al. Practice parameter update: management issues for women with epilepsy--focus on pregnancy (an evidence-based review): teratogenesis and perinatal

ISSN (O): 2687-5365; ISSN (P): 2753-6556

outcomes: report of the Quality Standards Subcommittee and Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology and American Epilepsy Society. Neurology 2009; 73:133–41.
7. Thomas SV, Indrani L, Devi GC, Jacob S, Beegum J, Jacob PP, et al. Pregnancy in women with epilepsy: preliminary results of Kerala registry of epilepsy and pregnancy. Neurol India 2001; 49:60–6.
8. Beach RL, Kaplan PW. Seizures in pregnancy: diagnosis and management. Int Rev Neurobiol. 2008; 83:259-71.
9. Li W, Hao N, Xiao Y, Zhou D. Clinical characteristics and pregnancy outcomes of new-onset epilepsy during pregnancy. Medicine (Baltimore) 2019; 98: e16156.
10. Alsfouk BA, Almarzouqi MR, Alsfouk AA, Alageel S, Alsemari A. Antiseizure medications use during pregnancy and congenital malformations: A retrospective study in Saudi Arabia. Saudi Pharm J 2021; 29:939–45.
11. Borthen I, Eide MG, Daltveit AK, Gilhus NE. Obstetric outcome in women with epilepsy: a hospital-based, retrospective study: Women with epilepsy and AED use show increased risk in pregnancy. BJOG 2011; 118:956–65.
12. MacDonald SC, Bateman BT, McElrath TF, Hernández-Díaz S. Mortality and morbidity during delivery hospitalization among pregnant women with epilepsy in the United States. JAMA Neurol 2015; 72:981–8.
13. Razaz N, Tomson T, Wikström A-K, Cnattingius S. Association between pregnancy and perinatal outcomes among women with epilepsy. JAMA Neurol 2017; 74:983.
14. Borthen I, Eide MG, Daltveit AK, Gilhus NE. Delivery outcome of women with epilepsy: a population-based cohort study: Delivery outcome in women with epilepsy. BJOG 2010; 117:1537–43.
15. Chen Y-H, Chiou H-Y, Lin H-C, Lin H-L. Affect of seizures during gestation on pregnancy outcomes in women with epilepsy. Arch Neurol 2009; 66:979–84.
16. Kashif T, Fathima N, Usman N, Qaseem A, Jayaraj JS. Women with epilepsy: Antiepileptic drugs and perinatal outcomes. Cureus 2019; 11: e5642.

ISSN (O): 2687-5365; ISSN (P): 2753-6556