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Maternal and perinatal outcome in pregnancy with epilepsy: A five year retrospective study

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Abstract
Background: Epilepsy is a common neurological disorder. Women with epilepsy tend to fear the effect the disease on their babies.
Objectives: The objective of the present study is to analyse the effect of epilepsy on the maternal and perinatal outcomes in pregnant women.
Method: A retrospective analysis of Medical Records of women with epilepsy admitted to the labour ward was done from the year 2015 -2020.
Results: A total of 17613 women delivered during the study period of which 41 patients were suffering from epilepsy. A total of six antiepileptic drugs were used of which the commonest one as monotherapy was Levetiracetam (48.8%). It was observed that 29.2% of the patients required polytherapy. Recurrent seizures were observed in 24.3% of the patients. Fourteen percent of the patients had a prior history of abortions. Of the obstetric complications 7.3%of the patients had pre-eclampsia and 36.6% had late preterm. There were no association with antepartum or postpartum haemorrhage. Small for gestational age was observed in 12.19% of the cases.
Conclusion: With the shift in the use of second generation AEDS like Levetiracetam for the treatment of pregnant women with epilepsy, the maternal and perinatal outcomes are promising.

Keywords: Maternal, epilepsy, pregnancy, perinatal, levetiracetam

Introduction
Epilepsy is a common neurological disorder, affecting 1% of the population in India. The prevalence of epilepsy at any point of time has said to be 6.38 per 1,000 persons [2]. Epileptic women during their reproductive age have a higher fear of the burden of the disease on pregnancy. Issues such as the increase in the frequency of seizures during pregnancy, effects of the anti-epileptic drugs (AED) on the foetus and effect of the seizure on the foetus tend to create anxiety among the epileptic women [3].
Various AEDs have been used in epilepsy. The older Antiepileptic drugs like Sodium Valproate, Phenytoin, Carbamazepine have been known to cause congenital malformations [4] Second generation AEDs have also been used. Of them Levetiracetam and Lamotrigine have been extensively studied. Other Second generation drugs such as Oxcarbamazepine, Zonisamide, Topiramate and Gabapentin have not been studied extensively. Newer generation AEDs i.e. those that were used from year 2000 such as lacosamide and eslicarbazepine, have limited experience in pregnancy [5]. Little is known regarding the pharmacokinetics of newer generation AEDs like pregabalin, lacosamide, retigabine, and eslicarbazepine acetate [6].
Teratogenic effects of the AEDs In a large-scale prospective study based on the EURAP international registry, it was observed 10.3% of the pregnant women on valproate, 6.5% on phenobarbital, 6.4%on phenytoin, 5.5%carbamazepine, 3.9% on topiramate 3% on oxcarbamazepine, 2.9% on lamotrigine and 2.8% on levetiracetam developed major congenital malformations [7].
The UK has banned the use of sodium valproate in women who are not in a pregnancy prevention program, due to the potential teratogenic effect on the foetus. Second generation AEDs Levetiracetam and Lamotrigine are being preferred over the older AEDs as they have lesser incidence of congenital malformations [4].

Epilepsy has been known to be associated with an increased incidence of maternal obstetric complications.). Women with epilepsy have an increased incidence of spontaneous miscarriage, antepartum haemorrhage, post-partum haemorrhage, hypertensive disorders, induction of labour and caesarean section [8].

Seizure during pregnancy can have adverse effects on the foetus. Even a single convulsion can cause foetal bradycardia for more than 20 minutes and repeated convulsions can cause foetal hypoxia, acidosis and foetal demise [9].

This study aims

1. To analyze the obstetric outcomes in pregnant women with epilepsy attending BLDE (DU) Shri BM Patil Medical College Hospital and Research Center Vijayapura, North Karnataka and Bhagavati Hospital over the last 5 years.
2. To study the perinatal outcomes in these patients.

Materials and Methods

Study design: Retrospective Observational Study

Source of data: The study was conducted in BLDE(DU) Shri BM Patil Medical college, Hospital and Research Centre, Vijayapura and Bhagavati Hospital. Shri BM Patil Medical College, Hospital and Research Centre is a Tertiary care Post graduate and undergraduate teaching Hospital and Bhagavati Hospital is a Multispeciality Hospital Catering to Neurology and OBGYN patients. The study was conducted from 2015 to 30th Sept 2020. The study has received Ethical Clearance from Institutional Ethic Committee BLDE(DU)/IEC/475/2020-21 The data was collected from the Medical records case files maintained at the hospitals. The data was entered in a proforma. All case sheets were analyzed and the information was entered in a proforma. Information regarding the history of spontaneous abortions, fetal malformations, obstetric complications, neonatal outcomes, treatment history regarding the use of Antiepileptic Drugs(AED) were analyzed.

Inclusion Criteria

1. All pregnant women who were diagnosed to have epilepsy at BLDE (DU) Shri BM Patil medical college and Bhagavati Hospital, Vijayapura
2. Women who were diagnosed to have epilepsy prior to the conception.

Exclusion Criteria

1. Any cause of seizures of other known origin like tuberculoma, tumors of the brain intracranial space occupying lesions etc.

Statistical analysis

Categorical variables were presented as frequency (%)

Results

During the study period a total of 17613 women delivered in the hospitals of which 41 patients were pregnant women with epilepsy. A majority of the patients were multigravidae. Most of the women were in their 2nd decade of age. Most of the women reached Term (92.7%) (Table1)

The commonest AED used to treat epilepsy in this study is Levetiracetam with nearly half of the patients receiving it. It was observed that 29.2% of the patients required polytherapy. Other drugs that were used were phenytoin, Carbamazepine and Clobazam. (Table2)

Of the patients on treatment 10 (24.3%) patients had recurrent seizures, of which 5 patients were on Levetiracetam, 2 on a combination of levetiracetam, phenytoin and valproate and 2 on carbamazepine and clobazam. All the women received Folic Acid supplements. None of the women received Vitamin K supplementation.

Of the 41 women with epilepsy 12(29.3%) had vaginal deliveries and 29(70.7%) had Caesarean Section.

Prior abortions were seen in 14 patients (31.4%). Preeclampsia was observed in 3 patients (7.3%).

Most of the babies born were term and of weight in the range of 2.5-3.5kgs (87.8%). There were no neonatal complications in the babies. No major congenital malformations were noted in these babies. All the women breast fed their babies. (Table 3)

Table 1: Demographics & gestational age of the participants.

Gravidity	No. of cases/ total cases	%
Primigravida	15/41	36.6
Multigravida	26/41	63.4
Age of the participants in years		
20-22	15/41	36.6
22-24	10/41	24.4
25-27	14/41	34.2
28-30	2/41	4.9
Gestational age of the participants		
36	3/41	7.3
38	16/41	39.0
39	16/41	39.0
40	4/41	9.8
41	2/41	4.9

Table 2: Various antiepileptic drugs used for treatment of epilepsy in the pregnant women

Name of the drug	No. of patients on treatment of the drug/total no. of patients	%
Levetiracetam	20/41	48.8
Phenytoin	5/41	12.2
Carbamazepine	2/41	4.9
Phenobarbitone	2/41	4.9
Levetiracetam with phenytoin	4/41	9.8
Levetiracetam with valproate with phenytoin	2/41	4.9
Levetiracetam with valproate	2/41	4.9
Carbamazepine with clobazam	2/41	4.9
Carbamazepine with phenobarbitone	2/41	4.9

Table 3: Weight showing the weight of the babies

Weight of the babies in Kgs	No. of babies/ Total no. Of babies	%
2-2.4	5/41	12.2
2.5-2.9	20/41	48.8
3-3.5	16/41	39.0

Discussion

The present study was done to analyse the maternal and foetal outcomes in women with epilepsy. In our study a majority of the women who continued pregnancy after an anomaly scan did reach term. Other studies showed that the incidence of preterm, still birth was not increased in epileptic women [4]. In our study, Levetiracetam was the most common monotherapy AED drug used. It was also used in polytherapy. Levetiracetam is a second-generation drug. It has been studied extensively and has found not to be associated with major congenital anomalies. Drugs such as Sodium Valproate, Phenytoin and Carbamazepine have been notorious in causing major congenital malformation [7, 9].

With the shift of use of 2nd generation AEDS Levetiracetam and Lamotrigine, new optimism has been observed by the women with epilepsy [10, 11]. Almost a fourth of the patients experienced recurrent seizures. In a study conducted in Emory epilepsy centre they found that despite the increase of the dose of AEDs during pregnancy, there was an increase in the seizures during pregnancy by 38.4% [12]. In the present study it was observed that 7.3% of the patients suffered pre-eclampsia. In a national level study conducted in Norway, they concluded that the risk of severe pre-eclampsia in women with epilepsy increased. They attributed this to the regular intake of folic acid in the women with epilepsy along with the AEDs [13]

Various studies have shown that epilepsy is associated with abruptio placentae, higher incidence of induction of labour and caesarean section, still births, small for gestational age, preterm births, low AGAR score, congenital malformations [14, 15]. On our study, there was no such increase in any of the complications except for a higher number of women undergoing caesarean section. This may be due to the fact that the studies are covering long periods of time and during such times there was usage of older AEDs.

Pre-pregnancy counselling is of utmost importance and can help to reduce the burden of the disease on pregnancy. Changing the AED can be considered prior to conception. Women should be made aware of the importance of folic acid supplementation, which had said to have reduced the congenital malformations in the foetus. Studies have shown that about half of the women with epilepsy had unplanned pregnancies [16].

Conclusion: With the shift in the use of second generation AEDS for the treatment of pregnant women with epilepsy, the maternal and perinatal outcomes are promising.

Limitations: This study did not take into account the pregnant women with epilepsy who terminated their pregnancies due to major congenital malformations.

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