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Fetomaternal Outcomes In Pregnancy Complicated By Epilepsy.

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ABSTRACT

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. This study is conducted to find out possible course and complications of epilepsy and its treatment in mother and fetus as many women will be anxious regarding this high-risk condition. This is a retrospective study conducted in department of obstetrics and gynaecology Department Of Obstetrics & Gynecology, Government Thiruvarur Medical College, Thiruvarur, Tamil Nadu , India. Out of a total of 100 deliveries during that period, we identified 64 patients with epilepsy complicating pregnancy. Antepartum, intrapartum and postpartum details of 36 patients whose data was available in electronic medical records was collected and analysed using SPSS 17 software. In this study we noted that the incidence of epilepsy was 0.009%. the 50% of patients were in 25-30 years agegroup. More than 98% were on long term antiepileptic drugs. Majority were on monotherapy, most commonly on leviteracetam and were well controlled with monotherapy. The 38.5% had recurrence of seizures during pregnancy, mostly in latter half of pregnancy. Patients with seizure free interval of 9 months prior to pregnancy did not have any further epilepsy episodes. The incidence of other medical and obstetric complications was found to be similar to general population. There was 10% incidence of IUGR and fetal anomaly. The seizures were well controlled with monotherapy and we found that generally pregnancy and deliveryis well tolerated and overall neonatal outcomes were good.

Keywords: Epilepsy, Seizure, pregnancy, Leviteracetam.

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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 motherland 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 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.

METHODS

It is a retrospective descriptive study in which the data of all booked antenatal patients diagnosed with epilepsy was collected from the labor records and electronic medical records. The details of these 64patients with epilepsy-like age, parity, type, years of seizure medications, seizure free interval before pregnancy, drugs used in pregnancy (monotherapy or polytherapy), seizure episode during pregnancy in each trimester, coexisting medical disorders like gestational diabetes, pregnancy induced hypertension and obstetric complications like preterm labor, PPROM, antepartum hemorrhage, mode of delivery, fetal outcomes like anomalies, birth weight; were collected. All babies were given injection vitamin K IM at birth as part of routine IAP protocol and also started breastfeeding soon after birth.

RESULTS

Out of 64 patients, majority were in 25-29-year age group (50.9%), 59% were multigravidas and 47.4% patients were on AED for 10-20 years. Only one patient was not on any AED as her last seizure episodes was 7 years back, hence the drug was withdrawn. During the antenatal period 22 patients (38%) had seizureepisodes with comparable incidence in all three trimesters-6 in 1st trimester (24%), 8 each in 2nd and 3rd trimester (36%each). We had one patient on polytherapy who had multiple uncontrolled seizures in all 3 trimesters with cause for same not identified and another patient who was on monotherapy had seizures in 2nd and 3rd trimester. The seizures subsided spontaneously postpartum after alteringthe dose of drug. 2 patients had intrapartum seizures and none happened in postpartum. Of the patients who had seizures during the antenatal period 17.5% patients needed revision and hiking anti- epileptic medications. On analysis of maternal data, 3 patients developed pregnancy induced hypertension and 4 developed GDM. None of the patients had obstetric complications like antepartum hemorrhage, PPROM or stillbirth. Over a half (54 %) of patient went for cesarean section because of various indication, most common being previous LSCS. The 84.3% were term deliveries while 15% were preterm deliveries.

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Table 1: Epilepsy characteristics.

Variables	Frequency	Percentage (%)
Duration of seizures medications (Years)		
<10	20	35.1
10-20	27	47.4
20	9	15.8
No AED	1	1.8
Type of seizures		
GTCS	44	77.8
Myoclonic	1	1.8
Complex partial	2	3.5
Status epilepticus	2	3.5
Others	8	14
Seizure free interval prior to pregnancy (years)		
<1	22	38.5
>1	28	49.1
Not available	7	12.4

Table 2: Epilepsy characteristics in pregnancy

Variables	Frequency	Percentage(%)
Drug treatment		
No drugs	1	1.7
Monotherapy	41	71.9
Levipil	20	48.7
Benzodiazepines	10	24.3
Carbamazepine	4	9
Others (like divalproex,lamtorigine)	7	17
Polytherapy	15	26.3
Incidence of seizures in pregnancy		
Antepartum	22	38.5
1st trimester	6	27
2nd trimester	8	36
3rd trimester	8	36
All 3 trimesters	1	
Intrapartum	2	3
Postpartum	0	
Pregnancy co-morbidities	7	12.2
GDM	4	7
PIH	3	5
Change in dose/medications		
Needed	10	17.5
Not needed	47	

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Table 3: Fetal characteristics

Variables	Frequency	Percentage(%)
Congenital anomalies	6/57	10.52
IUGR	7/57	10
Gestational age at delivery		
Pre term	9	15.7
Term	48	84.3
Mode of delivery		
Normal	26	45.6
LSCS	31	54.4
Sex of the baby		
Male	35	61.4
Female	22	38.6
Birth weight (kg)		
<2	6	10.5
2-2.5	7	12.3
>2.5	44	71.2

DISCUSSION

The 2.5 million Women in India suffer from epilepsy and 25% are in reproductive age group. Hence, addressing epilepsy in pregnancy is important. The review of literature suggested preference of monotherapy over polytherapy during pregnancy [3]. This is due to decreased risk of side effects and congenital anomalies due to synergistic effect of both the drugs. Even in our study, majority (77%) were well controlled with monotherapy with drugs like leviteracetam, benzodiazepines. Polytherapy was resorted to only when there was failure of monotherapy at maximum permissible doses. As per study by Robinson et al epilepsy has been associated with increased rates of cesarean section although the indication is not clear. Epilepsy itself is not an indication for cesarean section.[4] The study consisted of59% multigravidas and the rate of cesarean delivery in our study also of almost 54%. The most common indication identified was previous cesarean with mobile head. There is insufficient evidence of change in frequency of seizure episodes during pregnancy, as per American association of neurology, however Monead study stated that women who had a 9-month seizure free interval prior to pregnancy were less likely to have seizure episodes during pregnancy [5]. Recent study showed, use of leviteracetam is associated with increased seizure free interval and better outcomes while lamotrigine and carbamazepine had similar results [6]. In our study, majorityof the patients (49.1%) had seizure free period for more than 1 year prior to pregnancy and had hence had seizure free antenatal period. The study of neurological diseases in pregnancy stated incidence of intrapartum seizure to be around 3-4% [7]. In our study, we had 2 patients who had intrapartum seizures (3%). Both were managed with IV leviteracetam. There was one patient who was on polytherapy and had multiple episodes of epilepsy in ante partum and intrapartum period. This may be due to non-adherence to antiepileptic medications. One patient had multiple seizure episodes in second and third trimester; this could be due tochange in therapeutic levels of leviteracetam in pregnancy,which ideally needs to be monitored as seen in study by Mahajan et al [8]. However, RCOG does not currently recommend routine serum antiepileptic drug monitoring because of lack of its evidence on control of seizures.[7]In previous studies like by Goel et al there was 24.3% incidence of PIH and 2.7% incidence of GDM with epilepsy [9]. Overall it has been reported that there is higher. incidence of preeclampsia in patients with epilepsy complicating pregnancy especially on lamotrigine and carbamazepine [10]. In our study, though the incidence of GDM was comparable to around 7%; we got a lower incidence of PIH of around 5% only. It could be related to use of leviteracetam; however, there is no proven study. Due to increase in clearance rate of drugs during pregnancy, there is increased need for changing drug dosage and opting for higher doses. Almost 45% of patients needed change in drug dosage in our study. Postpartum, risk of epilepsy is 1-2% but in our study no incidence of postpartum seizure was noted.[7] This may be due to strict adherence to the antiepileptic medications. Major malformations have been associated with use of valproate as a monotherapy or polytherapy so should be avoided. Antiepileptic like lamotrigine and levetiracetam even in combination are equivalent to monotherapy in safety. Among newer drugs, lamotrigine is safest during pregnancy though when compared to general population still higher risk of congenital malformations is there. Topiramate has intermediate risk of

malformations with facial/palate cleft. Folic acid supplementation is recommended preconceptionally and during pregnancy at a minimum dose of 0.4 mg/day (4 mg/day if family history of neural tube defect, or on valproic acid, carbamazepine, or gabapentin) [5]. Epilepsy itself does not significantly increase risk of major congenital malformation. It is noted that risk of congenital malformation in women taking antiepileptic drug is 10% compared to general population [11]. In our study, congenital anomalies were seen in 10.5% of the study group most of which were correctable cardiac anomalies like SVT, VSD.As per previous studies, there is conflicting data on evidence of preterm delivery and SGA fetuses among women on antiepileptic and those without. In case of preterm deliveries, the cause has been attributed to seizure itself [12]. There is twofold increase in SGA babies amongst women on antiepileptic drugs compared to those not on any drugs [13]. In our study we had 10% babies with growth restriction and low birth weight. be useful for clinicians to counsel their patients about the prospective overall outcomes and management.

CONCLUSION

Pregnancy complicated by epilepsy is definitely a high- risk condition that needs multidisciplinary and careful management. Pre-conceptional counselling is very important in such patients and they should be counselled about optimizing the antiepileptic medications, importance of compliance and adhering to follow up to see for change of dose. Pre-conceptional counselling and folic acid is recommended for all women on antiepileptic medications at 0.4mg/day. If family history of neural tube defect is present, recommended dose is 4 mg/day. Monotherapy for epilepsy treatment has been associated with better fetomaternal outcomes in pregnancy. However, due to increased drug clearance in pregnancy, there is frequent need for changing of drug dosage. Lamotrigine and leviteracetam have been shown to be safest out of all the antiepileptic drugs in pregnancy in terms of fetal malformations and adverse fetal outcomes like NICU admission. Overall, generally pregnancy and delivery are well tolerated and overall neonatal outcomes are good if patient has a seizure free period before conception and epilepsy is well controlled.

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