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Original Article

Feto-maternal outcome in pregnancy with epilepsy in a tertiary care hospital

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Abstract

Objectives: Pregnancy with epilepsy is indeed high risk pregnancy. The purpose of this study was to evaluate the feto-maternal outcome based on the type of epilepsy and treatment offered. *Methods:* 49 pregnant women with epilepsy attending the antenatal clinic in a tertiary care hospital over a period of 3½ years were evaluated. *Results:* Out of the pregnant women with epilepsy in this study, 6 patients were lost to followup, liveborn infants were delivered in 41 out of 43 pregnant women. Out of the 41 liveborn infants major congenital malformations were observed in two babies and minor anomalies in three. The use of anticonvulsants in our study was carbamazepine in 19(44.18%), oxcarbazepine in 7(16.3%), phenytoin in 9(20.4%), valproate in 5(11.6%), lamotrigine in 3 patients (6.9%). *Conclusions:* Out of the 43 pregnant women with epilepsy in this study, fetal loss and major malformations were observed in 4.65% cases each.

Key words: pregnancy, epilepsy, feto-maternal outcome.

Introduction

Epilepsy is the second common chronic neurological disorder complicating pregnancy after migraine. About 2.5 million women in India suffer from epilepsy, with 52 of them being in the reproductive age group [1]. Incidence of seizure disorder in women attending antenatal clinics is estimated to be 0.3-0.5% of all births. These pregnancies are a challenge to patient and clinician alike, the double burden of seizures and the antiepileptic drugs (AED) exposure are responsible for the poorer outcome of infants born to mothers with epilepsy [2]. Majority of women with epilepsy will have normal, healthy infants. Effective preconceptional counseling and medical care is essential for the treatment of the pregnant women with epilepsy [3,4]. Exposure to AED has been associated with two to three times increase in major malformations in infants exposed in utero as compared to the ordinary population. We report an observational prospective study of fetomaternal outcome in pregnancy with epilepsy attending a tertiary care hospital.

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Methods

This study comprised of forty-nine mothers with

epilepsy who attended the antenatal clinics of our hospital. Those referred from epilepsy clinic of the Neuromedicine Department over a period of 3 ½ years were recruited in the study. The patients were thoroughly examined, assessed and monitored regarding the feto-maternal outcome. The study also includes the assistance of the Radiodiagnosis department for antenatal ultrasound and anomaly scan, the Cardiology department for the fetal echocardiography, and Biochemistry department for the alphafetoprotein levels and the serum concentrations of antiepileptic drugs. Those patients who attended the antenatal clinic with epilepsy were further monitored for different parameter assessment for the subsequent visits.

Results

Out of the 49 patients recruited in this study, 6 patients were lost to follow up. Out of the remaining 43 patients, liveborn infants were delivered in 41. One fetus was a stillborn and another was term intrauterine death (IUD). Out of the 41 live born infants major congenital defects were observed in two babies and minor anomalies in three babies.

Table 1 shows the age group breakup, the duration of epilepsy and the parity status. Table 2 shows the type of seizures and the timing of seizures during pregnancy. Only 6 episodes of seizures were documented during pregnancy and one episode during the postpartum period. Table 3 shows the antiepileptic drug used and the side effects. Major malformations were observed in 2 cases, one in phenytoin therapy, a cleft lip and one in valproate therapy, a spina bifida. Three minor anomalies were documented, one in carbamazepine therapy and two in phenytoin therapy. Table 4 shows the mode of delivery in these patients. The rate of Cesarean section is higher in these patients as they were high risk pregnancies with less fetal movements and also as some of the patients opted for the same. Table 5 shows the fetal outcome with two pregnancy losses, one an intrauterine death and one a stillborn. Prematurity was observed in 18.6%, low birth weight in 23.3%, intrauterine growth restriction and preterm labor in 9.3%. There was one case of birth asphyxia though the baby survived without need of ventilation. Five neonates (11.6%) had hyperbilirubinemia, one had Rh incompatibility and required exchange transfusion, another a case of ABO incompatibility needed photo therapy, three were cases of aggravated physiologic hyperbilirubinemia. All the neonates received intramuscular Vitamin K after delivery.

Table 1. Age group, parity, and duration of epilepsy .

Age Group (years)	Pregnancy with Epilepsy (n=43)	Duration of epilepsy A:-<1yr; B:- 1-<2yrs. C:->2-<4yrs.; D:->4yrs.	Parity (n=43)
16-24	5(11.6%)	A-1, B-4	P0-3, Pl-1; P2-1
>24-<28	23(53.5%)	A-2, B-14, C-4, D-3	P0-15, Pl-5;P2-2,P3-1
>28-<32	13(30.2%)	A-2, B-8, C-3	P0-9; P1-2, P2-2
>32	2(4.6%)	B-2	P0-1; P1-1
Total	43	A-5, B-28, C-7, D-3	P0-28;Pl-9; P2-5; P3-1.

Table 2. The pattern of epilepsy and time of seizures of the pregnant epileptic women.

Pattern of Epilepsy	Distribution & Percentage	Timing of Seizures (First trimester (1T); Second trimester (2T); Third trimester (3T) Postpartum (PP)
Generalized Tonic and Clonic seizures	24 (55.8%)	1 1T, 1 2T, 1 3T, 1 PP
Partial seizures	7 (16.3%)	1 1T, 1 2T
Complex Partial seizures	2 (4.65%)	
Absent seizures	8 (18.6%)	1 1T
Mixed seizures	2 (4.65%)	
Total	43	3 1T, 2 2T, 1 3T, 1 PP

Table 3. Anti-epileptic drugs and outcome.

Antiepileptic drugs	Usage & percentage	Malformation (M-Major, m-minor)
Carbamazepine	19 (44.2%)	1m
Oxcarbamazepine	7 (16.3%)	
Phenytoin	9 (20.9%)	1M, 2m
Valproate	5 (11.6%)	1M
Lamotrigine	3 (6.9%)	

Table 4. Mode of delivery.

Parameters	Number (N-43)	Percentage
Vaginal	11	25.58
Forceps	3	6.9
Ventouse	1	2.3
Cesarean section	28	65.1

Table 5. Fetal outcome.

Parameters	Pregnancy with epilepsy (N-43)	Percentage
Weight at birth	2.77±0.67 kg	
Pregnancy loss	2	4.6
Apgar at 1 min	7.29±0.98	
Apgar at 5 min	9.02±0.75	
Prematurity	8	18.6
Intrauterine growth restriction	4	9.3
Low birth weight	10	23.3
Preterm labor	4	9.3
Neonatal death	0	0
Birth asphyxia	1	2.3
Hyperbilirubinemia	5	11.6

Discussion

Pregnancy in a mother with epilepsy brings about several concerns including the risk of recurrent seizures, seizure aggravation, changes in drug levels because of altered pharmacokinetics and medication compliance and also because of the potential teratogenic effect of the AEDs [1,2]. Ideally effective preconceptional counseling and preparation must be done and importance of planned pregnancy is to be emphasized. After the diagnosis of pregnancy the regimen should be reassessed and monotherapy rather than polytherapy should be prescribed to minimize the risk of complications.

Pregnant women with epilepsy have a 4-8% chance of giving birth to a child with a major malformation as compared to only 2 to 4% of the general population [3-5]. Frequency of seizures is increased during pregnancy in one-third of women with epilepsy [2,3]. Major malformations are defined as defects of medical, surgical or cosmetic importance [3,4]. The type of anomalies occurring in infants born to pregnant women with epilepsy are orofacial clefts, cardiac diseases and neural tube defects which affects the child's life seriously. In pregnant mothers with epilepsy on one AED this occurs in 4 to 8% and is probably greater in those receiving more than one AED [5,6]. Minor anomalies seen are features of hypertelorism, epicanthal folds, shallow philtrum, distal digital hypoplasia, simian creases observed in 7 to 15% of infants exposed to antiepileptic drugs that represent a nearly two fold increase as that in the general population [4,6]. Many of these minor defects are idiopathic in nature and are only of a cosmetic concern.

Out of the 41 live born babies in this study, major congenital malformations were observed in two babies (4.87%) and minor anomalies in three (7.3%) which is comparable to other studies. Women with epilepsy have a 4 to 8% chance of giving birth to a child with major malformation compared with 2 to 4% in the general population [2,3,5]. The older antiepileptic drugs cause teratogenic effects by free radical production and folate deficiency and the risk is compounded in women receiving multiple AEDs [1,6]. Valproate demonstrates dose dependent serious adverse effects [6]. Folate supplementation was given in the preconceptional period and during gestation to all the women. Alphafetoprotein estimation at 16 to 18 weeks along with ultrasound for fetal anomaly were done in all the patients. The anticonvulsants used in our study were carbamazepine in 19(44.18%), oxcarbazepine in 7(16.3%), phenytoin in 9(20.9%), valproate in 5(11.6%) lamotrigine in 3 patients (6.9%). Studies with newer drugs like lamotrigine and oxcarbazepine show that the incidence of major malformations are not higher than with the older AEDs [7].

In our study there were two pregnancy losses (4.6%). Other studies show a twofold increase in late fetal loss from 2 to 7% of all pregnancies compared to 2 to 14% in pregnancy with epilepsy [5,6]. We have strongly

advocated breastfeeding in these 41 live born infants and 35 had exclusive breast feeding for 6 months. Neonatal bleeding can occur in mothers taking AEDs because of diminished amount of Vitamin K dependent clotting factors [8,9]. Ten women took vitamin K during the last month of pregnancy. No case of neonatal bleeding was observed in this study.

Conclusion

Pregnancy with epilepsy presents a unique challenge both for the mother and her baby. In this study we observed that though pregnancy with epilepsy needs comprehensive antenatal care and this results in uneventful pregnancies with good feto-maternal outcome. These women should be managed with monotherapy at the lowest possible dosage to diminish the risk of complications and also maintain good seizure control. They must be screened for alphafetoprotein levels and drug levels at 15 to 20 weeks and subjected to high-definition anomaly ultrasound scan at 18-20 weeks. These women should be managed with mandatory folate supplementation and the neonates must be given Vitamin K. These high risk pregnancies need spontaneous referral to tertiary care centers for better maternal and neonatal outcome. The perinatal complications can be diminished by the close coordination between the neurologist, obstetrician and the pediatrician.

References

1. Thomas SV. Management of epilepsy and pregnancy. J Postgrad Med 2006;52:57-64.
2. Morrel MJ. Epilepsy in women. Am Fam Physician 2002;66:1489-94.
3. Nathan J. Women with epilepsy. J Obstet Gynecol India 2004;54:543-53.
4. Jeha LE, Morris HH. Optimizing outcomes in pregnant women with epilepsy. Cleve Clin J Med 2005;72:938-45.
5. Morel MJ. Epilepsy and pregnancy: minimizing the risks. Contemp Ob Gyn 2004;49:51-70.
6. Meador KJ, Baker GA, Finnell RH et al. In utero antiepileptic drug exposure: fetal death and malformations. Neurology 2006;67:407-12.
7. Holmes LB, Harvey EA, Coull BA et al. The teratogenicity of anticonvulsant drugs. New Engl J Med 2001;344:1132-8.
8. Meador KJ, Zupanc ML. Neurodevelopmental outcomes of children born to mothers with epilepsy. Cleve Clin J Med 2004;71:38-41.
9. Yerby MS, Kaplan P, Tran T. Risks and management of pregnancy in women with epilepsy. Cleve Clin J Med 2004;71:25-37.