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A Study on Maternal and Perinatal Outcome in Epilepsy Complicating Pregnancy

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Abstract
Background: *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.*
Materials and Methods: *This was a descriptive study conducted in the antenatal outpatient clinic, antenatal wards and labour room of a tertiary care hospital over a period of one year. All pregnant women with pre-existing or recently diagnosed epilepsy after 20 completed weeks of gestation, a total of 126 patients were recruited. All patient details were collected using a structured questionnaire after getting their consent. Data were analysed using SPSS version 17.0 to obtain Chi square test and p value. The significance of the findings were interpreted.*
Result: *126 pregnant WWE were studied over a period of one year. Among women on AED 51.7% had seizures and 46% had statistically significant increase in frequency of seizures while women not on AED had 23% seizure and 20.6% had increased frequency of seizures during pregnancy. IUGR was statistically significant in AED group. Emergency CS 25.6% was statistically significant in AED group as compared to 10.3% among non- AED group, which could be due to higher induction rates among AED group.*
Conclusion: *Risk of maternal and fetal complications can be reduced with effective preconceptional planning, careful management during antenatal and post partum period.*
Keywords: *WWE women with epilepsy, AED anti epileptic drugs.*

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. 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[1]. Neurologists and obstetricians are increasingly faced with WWE during pregnancy. Majority of WWE who become pregnant have uncomplicated pregnancies and

deliver healthy infants. Experimental and clinical studies have shown that seizures are influenced by female sex hormones, estrogen and progesterone. Hence in about 1/3rd seizures worsen and in the rest 2/3rd they either reduce or remain unchanged. So the management issues that need to be addressed in these pregnancies include pre-conceptional folic acid supplementation, the teratogenecity of anticonvulsant medication, obstetric complications, infant cure, breast-feeding, contraception and the long term outcome for WWE [2].

The preconception management is the cornerstone in epilepsy care in WWE. A careful reappraisal of each case should ascertain the diagnosis, need for continued AED therapy, selection of appropriate AEDs, optimization of dosage and prescription of folic acid. During the pregnancy, the feta status need to be monitored with estimation of alphafetoproteins [AFP], and ultrasonography. Minor variations in anthropometric features have been observed in infants. Several institutions recommend oral vitamin K towards the end of pregnancy when enzyme inducing AEDs are prescribed because the later may potentially predispose the newborn to hemorrhagic disease, but recent reports indicate that such a risk is practically negligible. Besides WWE need to know that enzyme inducing AEDs may lead to failure of oral contraception.[1]

Materials and Methods

This was a descriptive study conducted in the antenatal outpatient clinic, antenatal wards and labour room of a tertiary care hospital over a period of one year. All pregnant women with pre-existing or recently diagnosed epilepsy after 20 completed weeks of gestation, a total of 126 patients were recruited. All patient details were collected using a structured questionnaire after getting their consent. Demographic parameters like age, parity, socioeconomic status, education, occupation, etc. were noted. The onset and type of epilepsy was noted. Detailed neurological history was taken. Details about preconceptional counselling, periconceptional folic acid and regularity of antenatal checkups were assessed. Antenatal complications were looked for in every visit. Details of seizure characteristics and AED changes were studied. Routine blood and radiographic investigations were done. Antenatal corticosteroids were given routinely to all cases presenting with preterm labour. Onset of labour was noted-whether spontaneous, induced or an elective Caesarian section. Induction was needed in some cases for various obstetric indications.

Labour was watched for progress, fetal distress, MSAF, seizures, and PPH. Mode of delivery was noted. After delivery, a detailed neonatal examination was done— Apgar score, birth asphyxia, birth weight, gestational age, anomalies, and hemorrhagic diseases were excluded. NICU admissions were sought and noted when needed. All perinatal deaths were recorded. Patients were discharged on the 3rd day after vaginal delivery. Only those who had undergone caesarean section or whose babies required observation or NICU admission stayed back.

Data were analysed using SPSS version 17.0 to obtain Chi square test and p value. The significance of the findings was interpreted.

Results

Demographic variables

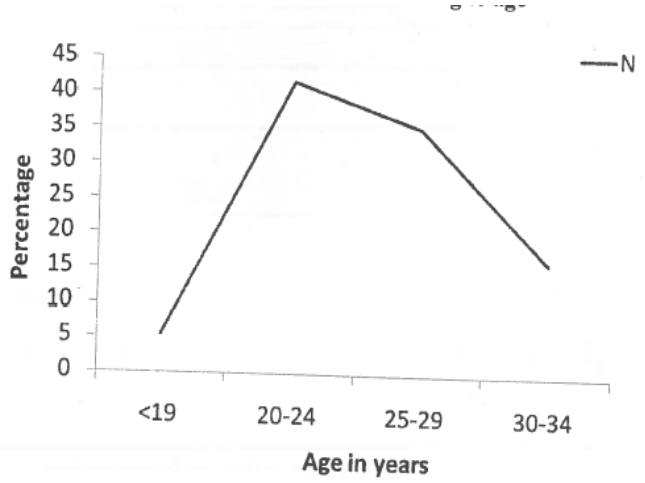

Figure 1: Distribution according to age

42.1% of patients belonged to 20-24 years age group followed by 35.7% to 25-29 years age group. Mean age was 25.35 years and Standard deviation was 4.2.

Table 1: Distribution according to educational background

Education	N	Percentage
Primary	11	8.7
High School	73	57.9
PDC	20	15.9
Degree and above	22	17.4
Total	126	100.0

Majority of my patients [57.9%] had high school education.

Table 2: Distribution according to parity

PARITY	N	Percentage
Primi	77	61.1
Para l	42	33.3
Para 2	5	4.0
>Para 3	2	1.6
Total	126	100.0

Majority of women 61.1% belonged to primipara group followed by parity 1.

Table 3: Distribution according to vitamin K prophylaxis

Vit K taken	Frequency	Percent
Taken	95	75.4
Not taken	31	24.6
Total	126	100.0

Vitamin K was taken in 75.4% women and all of them were on AED either antenatally or when reported in labour.

Table 4: Distribution according to maternal antenatal complications

Antenatal complications	AED		No AED		Total		**X2**	**P**
	N	**%**	N	**%**	**N**	%		
Hyperemesis	7	8.0	3	7.6	10	7.9	0.00	0.90
Threatened abortions	3	3.4	0	0	3	2.3	1.38	0.24
UTI	9	10.3	4	10.2	13	10.3	0.00	0.98
Abruption	1	1.1	0	0	1	0.7	0.45	0.50
IUGR	13	14.9	1	2.5	14	11.1	4.17	0.04
GDM	8	9.2	5	12.8	13	10.3	0.38	0.58
GHTN	11	12.6	5	12.8	16	12.6	0.00	0.97
Placenta preavia	0	0	1	2.5	1	0.7	2.25	0.13
Infections	1	1.1	1	2.5	2	1.6	0.46	0.79
Breech	2	2.3	1	2.5	3	2.3	0.01	0.12
Oligohydramnios	8	9.2	6	15.4	14	11.1	1.04	0.31
Polyhydramnios	3	3.4	1	2.5	4	3.1	0.07	0.79

UGR was more in women in AED as compared to the no AED group which was statistically significant.

Table 5: Distribution according to onset of labour

Onset of labour	AED		No AED		Total		**X2**	**P**
	N	**%**	N	**%**	**N**	%		
Spontaneous	40	46.0	20	51.3	60	47.6	0.30	0.58
Induced	38	43.7	9	23.1	47	37.3	4.89	0.02
Elective CS	9	10.3	10	25.6	19	15.1	4.92	0.02
Total	87	100	39	100	126	100		

Induction of labour was 43.7% in the AED group and elective CS was 25.6% in the no AED group which were statistically significant.

Table 6: Distribution according to mode of delivery

Mode of delivery	AED		No AED		Total		**X2**	**P**
	N	**%**	N	**%**	**N**	%		
Vaginal	49	56.3	22	56.4	71	56.3	0.00	0.99
Instrumental	3	3.4	2	5.2	5	3.9	0.21	0.65
Elective CS	9	10.4	10	25.6	19	15.0	4.92	0.02
Emergency CS	26	29.9	5	12.8	31	24.7	4.23	0.04
Total	87	100	39	100	126			

Emergency CS was 29.9% in the AED group which was statistically significant.

Table 7: Distribution according to neonatal variables

Bwt in kg	AED		No AED		Total		X2	P
	N	%	N	%	N	%		
Birth asphyxia	6	6.8	4	10.3	10	7.9	0.42	0.51
Apgar score <7@5'	8	9.2	0	0	8	6.3	3.74	0.05
NICU admission	11	12.6	5	12.8	16	12.7	0.00	0.97
Neonatal infection	2	2.3	3	7.6	5	4.0	2.06	0.15
Hemnorrhagic disease	1	1.11	1	2.6	2	1.6	0.34	0.55
Hyperbilirubinemia	11	12.6	6	15.4	17	13.5	0.17	0.67
Anomalies	10	11.2	3	7.6	13	10.3	0.42	0.51

Among the studied newborn variables only Apgar Score <7 at 5 were statistically significant in the WWE on AED.

Discussion

Demographic variables

42.1% and 35.7% of patients in the study belonged to 20 to 24 and 25 to 29 year age group, with a mean age of 25.35 years. 93.7% of the women were housewives, who belonged to low socioeconomic status 62.7%. 57.9% of women were educated up to high school 61.1% of my patients were primiparas.

Epilepsy parameters

In the present study 56.3% patients had h/o childhood onset of epilepsy. 80.1% of women had localized type of epilepsy of which complex partial seizures were more common followed by simple partial seizures. Primary generalized seizures were present in 19.9% which included 4 cases of JME. Women with JME only one was on VPA others were on other AED.

Maternal variables

In this study there were 8% patients who had preconceptional counseling. There is no evidence to inform the content, methods of delivery or effectiveness of preconception counseling to improve pregnancy outcomes for WWE and their offspring. In the present study, the WWE were divided into AED and no AED groups and further into those on monotherapy and those on polytherapy according to the intake during their periconceptional period. It was noted that there were 69% of WWE un AED [59.5% were on monotherapy, 9.5% on polytherapy of the total women in study] and 31% were not on AED.

Periconceptional folic acid was only taken by 34.4% of women on AED and only 7.6% of not on AED which was significant. This is mainly because of lack of preconceptional care.

In my study antenatal seizures were present in 51.7% of women on AEDs and that noted in WWE not on AED was only 23% which was significant.

In this study, WWE irrespective of AED use, there was 38% increase, 49.4% no change and 12.6% decrease in seizure frequency. WWE on AED also showed a significant increase [46%] in seizure frequency when compared to those not on AED [20.6%]. 18.4% had a decrease and 3 5.6% had no change in seizure frequency in women on AED. 79.4% women not on AED had no change in seizure frequency. Women on monotherapy had a 48% increase, 16% had a decrease and 36% had no change in seizure frequency. Women on polytherapy had a 33.3% increase, 33.3% had decrease and 33.3% had no change in seizure frequency but was not statistically significant. Most of the seizures occurred due to drug default.

In this study Vitamin K was taken in 75.4% women and all of them were on AED. These patients were administered the vitamin K either in the antenatal period in third trimester, when admitted or at the onset of labour. Current report states that there also was no evidence to support or refute taking vitamin K in WWE on maternal enzyme-inducing AED [Aleksey 2010].

Regarding maternal obstetric complications, in my study there was the following complications: IUGR [11.1%], GHTN [12.6%], GDM [10.3%],

hyperemesis [7.9%], h/o threatened abortion [2.3%], UTI [10.3%], oligohydramnios [11.1%], polyhydamnios [3.1%], abruption [0.7%], breech [2.3%], placenta praevia [0.7%] in WWE. Among them IUGR was statistically significant in the AED group, the rest were comparable in both groups.

In this study, 56.3% women had a vaginal route of delivery in both groups and 39.7% had a CS, in which the emergency CS rates were statistically significant in the WWE on AED, all were done for obstetric indications. This could be due to higher induction rates. 3.9% Instrumental deliveries were seen in WWE in this study which is similar to a study in Canada which reported that same [Richmond et al. 2004].

New born variables

In my study 88.1% of women had a term gestation and 11.9% were preterm. AED may cause preterm birth through drug induced folate deficiency [Steegers-Theunissen RP 1994], through depression of thyroid function [Kaneko S 1991] or through epoxide formation [Jones KL 1989]. In this study, preterm delivery were noted in 11.5% and 12.8% in the AED and no AED groups, none was statistically significant. One reason that preterm labour may be higher in this study is that a large majority of patients belong to the low socioeconomic group.

In this study 6.3% of babies had a poor Apgar score [<7 @ 5 all of which belonged to the AED group and was statistically significant. This was mainly seen in preterm deliveries. In this study there was 10.3% anomalies in WWE, it was comparable in both the AED [11.2%] and no AED [7.6%] groups.

Conclusion

Careful planning and management of any pregnancy in WWE is essential to increase the likelihood of a healthy outcome for mother and infant.

Although women who have epilepsy and are taking AEDs do have increased risks for maternal and fetal complications, these risks can be reduced with effective preconceptional planning and careful management during pregnancy and the postpartum period.

Although in this study majority of the women had a favourable outcome, maternal obstetric complications and anomalies were seen. Preconceptional counseling was inadequate. IUGR was noted significantly more in WWE on AED. Induction rates were significantly more in WWE on AED so was the emergency CS rates. Among the newborn variables APGAR score<7 @ 5' was statistically significant in the AED group. Supplement of folic acid periconceptionally and during pregnancy and use of AEDs with less potential for teratogenicity may help reduce the incidence of malformations. Educational efforts should be targeted to improve the management. A team effort including obstetrician and neurologist can ensure a healthy and fruitful life.

Summary

- Total of 126 WWE were included during one year study.
- 56.3% had childhood onset of seizures followed by adolescence onset.
- Majority of had localization type of epilepsy of which complex partial seizures were more common followed by simple partial seizures. There were also 4 cases of JME.
- Preconceptional counseling had been taken only by 8%.
- Regular health seeking behaviour was noted in 93.7%.
- Periconceptional folic acid intake was seen only in 22.2% overall in WWE.
- Outcome were analysed in those on AED[69%] and those not on AED (31%),they were further divided in those on monotherapy (59.5% of all WWE] and those on polytherapy [9.5%] according to periconceptional AED intake.
- Antenatal seizures were present in 43.2% of WWE almost similar to some studies. 51.7% of women on AEDs and 23% in WWE not on

AED had antenatal seizures, which was significant. Though there was no difference with respect to monotherapy and polytherapy.

- WWE on AED also showed a significant increase [46%] in seizure frequency when compared to those not on AED [20.6%]. There was no difference with respect to monotherapy and polytherapy.
- There were no cases of status epilepticus in the study.
- 66.6% of WWE did not have a change in AED/dose. In WWE not on AED 6.3% had to be started on monotherapy and 0.7% had to be put on polytherapy. In the monotherapy group, 5.5% had to be put on polytherapy. All WWE on polytherapy continued the same. 19.8% of WWE had to increase the dose of AED.
- Among the antenatal complications IUGR was statistically significant in the AED group, the rest were comparable in the other groups.
- Vitamin K was given to 75.4% women and all of them were on AED. These patients were administered the vitamin K either in the antenatal period in third trimester, when admitted or at the onset of labour. .,-
- Overall induction rate was 37.3% in WWE. Induction rate was statistically significant in the AED group [43.7%] as compared to the no AED group [23.1%] the most common reasons were GHTN, IIJGR, and oligohydramnios.
- Elective CS were significantly higher [25.6%] in no AED group when compared to the AED group [10.3%] most of it was for previous CS with 1° CPD.
- 56.3% women had a vaginal route of delivery in both groups and 39.7% had a CS, in which the emergency CS rates were statistically significant in the WWE on AED, all were done for obstetric indications, could be due to higher induction rates.
- 88.1% of WWE had a term gestation and 11.9% were preterm delivery. None were significant in AED/ no AED/ monotherapy/ polytherapy. One reason that preterm labour may be higher in this study is that a large majority of patients belong to the low socioeconomic group.
- 8.4% postpartum seizures were noted which were comparable in all groups. These were due to sleep deprivation and drug default.
- 1ntrapartum and postpartum maternal complications were comparable in mono/polytherapy groups.
- Birth weights were comparable in AED/AED and mono/ poly groups with a mean of 2.9 kg.
- 6.3% of babies had a poor Apgar score [<7 5'] all of which belonged to the AED group and was statistically significant, but that in the monotherapy/polytherapy groups were comparable.
- NICU admission [12.5%], birth asphyxia [7.9%], neonatal infections [4%] and haemorrhagic disease [1.6%] were comparable in all groups.
- In this study there was 10.3% anomalies in WWE, it was comparable in both the AED and no AED groups, but statistically significant in the polytherapy group 33.3% when compared to 8% of monotherapy group.
- All the anomalies noted in the no AED group were ASD. CBZ was one of the drugs in all WWE of polytherapy group with anomalies. Phenobarbitone and CBZ were the drugs taken by WWE in the monotherapy group.
- Perinatal death was 4% of total births, 2.4% were NNDs all of which belonged to the monotherapy group, 1.6% IUD, all of which belonged to the polytherapy group [16.6%] and was significant.
- NNDs were- congenital diaphragmatic hernia, anencephaly and irieningomyelocoele with CSF leak.
- Mean duration of hospital stay after delivery was 6.5 days, it was comparable in AED and no AED groups but significant in polytherapy 4 group [16.6%] due to preterm and anomalous babies.

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