



## Women with Epilepsy: Comparison between Monotherapy and Polytherapy in 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.*

**Aim of Study:** *To describe the obstetric and perinatal outcome of women with epilepsy with respect to those on monotherapy and polytherapy of antiepileptic drugs*

**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.*

**Results:** *126 pregnant women with epilepsy diagnosed before or during pregnancy were studied. Of these, 87 were taking anti-epileptic medications. 59.5% were on monotherapy and 9.5% on polytherapy AED. Childhood onset was most common [56.3%] followed by adolescent age of onset. (30.2%) 13% had adult onset epilepsy. 7% women who were not on AED had to be started on AED {mono plus poly}. 19.8% women had to increase their AED dose during pregnancy. 66.6% had no change. All the maternal antenatal complications studied in the monotherapy/polytherapy groups were comparable*

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

**Keywords:** *women with epilepsy (WWE), 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.

Hormonal and other factors can alter the pharmacokinetics of AED during pregnancy and puerperium. Antenatal exposure to AED, particularly at a higher dose and polytherapy increases the risk of fetal malformation. Recent reports raise the possibility of selective developmental language deficits and neurocognitive deficits with AEDs.

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 teratogenicity of anticonvulsant medication, obstetric complications, infant care, breast-feeding, contraception and the long term outcome for WWE]<sup>2</sup>. Their pregnancies and their unborn babies<sup>3</sup>

The preconception management is the cornerstone. 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 fetal status need to be monitored with estimation of alpha-fetoproteins [AFP], and ultrasonography.

There has been considerable progress in epilepsy care in the recent past. Several new AEDs with more favorable efficacy and less adverse effect profile, have been released. Surgical therapy of epilepsy has matured into a distinct, safe, and effective procedure of choice in selected cases of medically intractable epilepsy. The goal of

treatment now focuses on improved quality of life rather than mere control of seizures<sup>6</sup>.

### Materials and Methods

**Aim of Study:** To describe the obstetric and perinatal outcome of women with epilepsy with respect to those on monotherapy and polytherapy of antiepileptic drugs

**Study Setting:** 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. 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. Details of seizure characteristics and AED changes were studied. The cases were divided in terms of intake of AED during the periconceptional period and they were further divided in terms of number of AED taken — single drug as monotherapy and more than one drug as polytherapy. Data were analysed using SPSS version 17.0 to obtain Chi square test and p value. The significance of the findings were interpreted.

### Results

- A. 126 pregnant women with epilepsy diagnosed before or during pregnancy were studied. Of these, 87 were taking anti-epileptic medications. 59.5% were on monotherapy and 9.5% on polytherapy.
- B. The most commonly used drug was levitracetam.
- C. Onset of epilepsy:

Childhood onset was most common [56.3%] followed by adolescent age of onset. (30.2%) 13% had adult onset epilepsy. (Figure 1)

A) **Type of epilepsy:** Complex partial type was the most common diagnosis (47.6%)

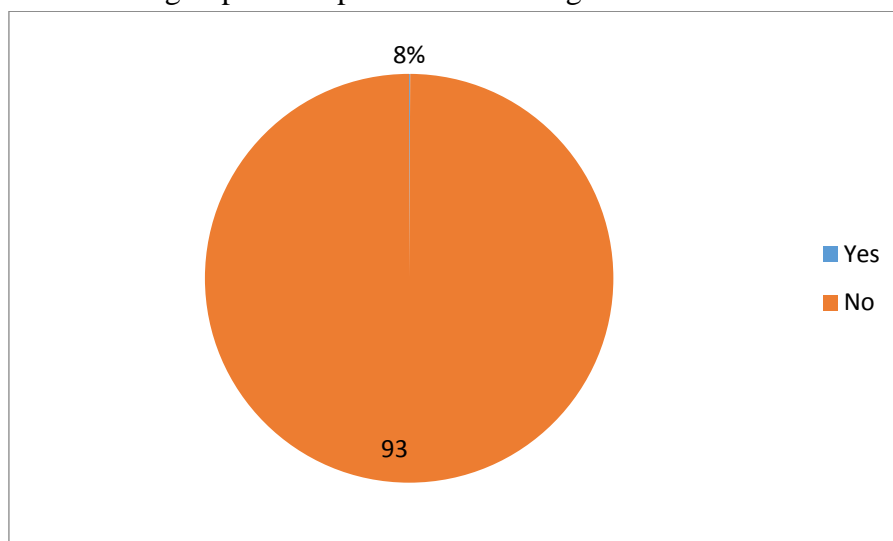
followed by simple partial type (26.5%) There were also 4 cases of JME. (table 1)

**Table 1:** Distribution according to type of epilepsy

Type of epilepsy		Frequency	Percentage
Localization type seizures	Simple partial seizure	33	26.5
	complex partial seizure	60	47.6
	Partial seizure with secondary generalization	8	6.3
Primary generalized seizures	Tonic clonic	19	15.1
	Clonic	1	0.8
	JME	4	3.2
Unclassified		1	0.8
Total		126	100.0

B) **Preconceptional counselling** Only 8% women had preconceptional counseling. (figure 2).

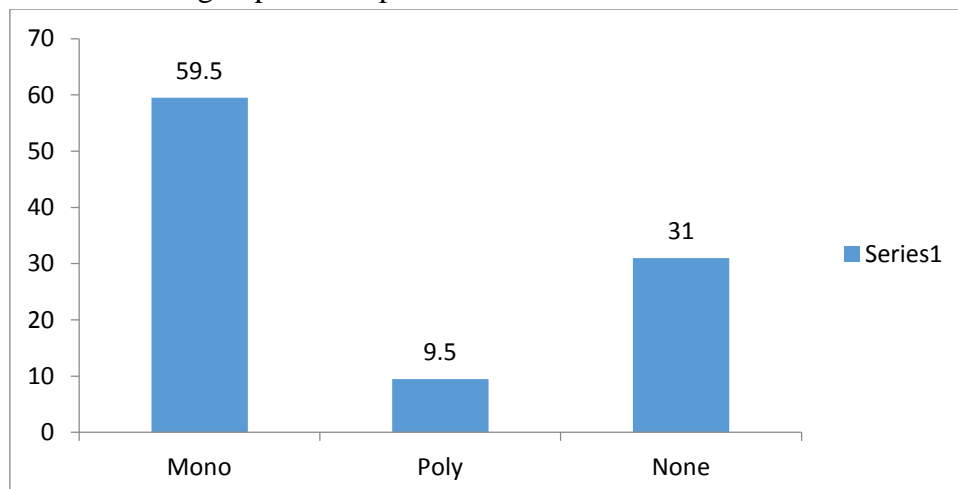
**Figure 2:** Distribution according to preconceptional counselling



C) **Anti-epileptic drug use periconceptionally:** 69.0% WWE took AED periconceptionally. 59.5% were on monotherapy and 9.5% on

polytherapy, of the total WWE. 31% were not on AED (figure 3)

**Figure 3:** Distribution according to periconceptional AED



**D) Health seeking behaviour:** Majority of patients were on regular antenatal checkups. (table 2)

**Table 2:** Distribution according to health seeking behaviour

Antenatal check up	Frequency	Percentage
Regular	118	93.7
Irregular	8	6.3
Total	126	100.0

**E) Seizure during this pregnancy:** 51.7% of WWE on AED had seizure during this pregnancy as compared to 23% of WWE who

were not on AED which was statistically significant. (table 3)

**Table 3:** Distribution according to seizure during this pregnancy

Seizure during pregnancy	AED		No AED		Total		X <sup>2</sup>	P
	N	%	N	%	N	%		
Present	45	51.7	9	23.0	54	42.9	10.68	0.001
Absent	42	48.3	30	77.0	72	57.1		
Total	87	100.0	39	100.0	126	100		

**F) Seizure frequency during this pregnancy:** Increasing seizure frequency was 46% in women on AED as compared to only 20.6% noted in women not on AED which was statistically significant. Seizure frequency

remained the same in 79.4% of women not on AED as compared to 35.6% in those on AED which also was statistically significant. (table 4)

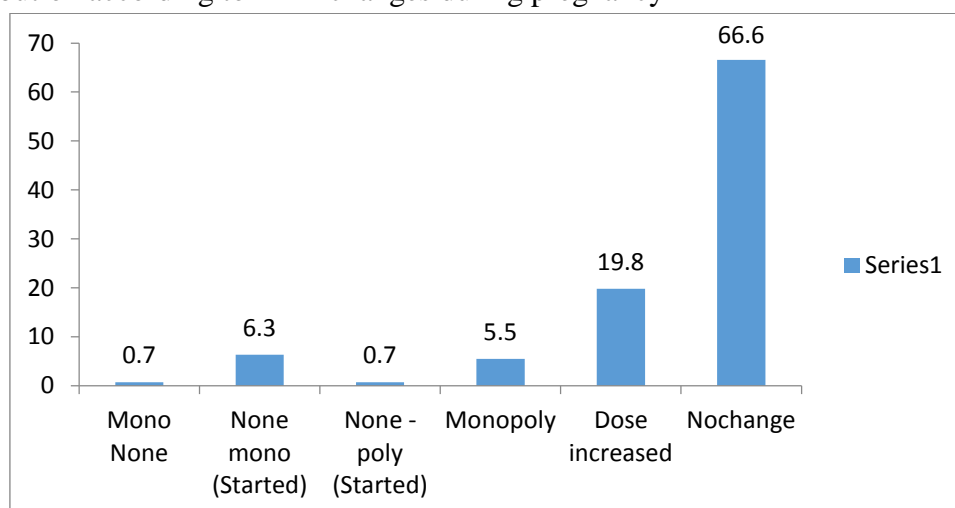
**Table 4:** Distribution according to seizure frequency during this pregnancy

Seizure during pregnancy	AED		No AED		Total		X <sup>2</sup>	P
	N	%	N	%	N	%		
Decreasing	16	18.4	0	0.0	16	12.6	2.41	0.12
Increasing	40	46.0	8	20.6	48	38.0	8.22	0.004
Same	31	35.6	31	79.4	62	49.4	20.72	0.001

**G) AED changes during pregnancy:** 7% women who were not on AED had to be started on AED {mono plus poly}. 19.8% women had to

increase their AED dose during pregnancy. 66.6% had no change. (figure 4).

**Figure 4:** Distribution according to AED changes during pregnancy



**H) Seizure frequency antenatally**

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. 18.4% had a decrease and 35.6% had no change in seizure frequency in women on AED. 79.4% women not on AED had no change in seizure frequency.(refer table 5)

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.

**Table 5**

Variable	Monotherapy		Polytherapy		X <sup>2</sup>	P
	N	%	N	%		
Seizure during pregnancy	39	52	6	50	0.02	0.89
Increased seizure frequency	36	48	4	33.3	0.90	0.34
Increased drug dose	30	40	2	16.6	2.42	0.11

**D) Antenatal complications:** All the maternal antenatal complications studied in the monotherapy/polytherapy groups were comparable (refer table-6)

**Table – 6** Comparison Between Monotherapy and Polytherapy regarding antenatal complications.

Variable	Monotherapy		Polytherapy		X <sup>2</sup>	P
	N	%	N	%		
Hyperremesis	6	8	1	8.3	0.00	0.96
Threatened abortions	3	4	0	0.0	0.50	0.48
UTI	8	10.6	1	8.3	0.06	0.80
Abruption	1	1.3	0	0.0	0.16	0.68
IUGR	11	14.6	2	16.6	0.03	0.85
GDM	7	9.3	1	8.3	0.11	0.91
GHTN	10	13.3	1	8.3	0.23	0.62
Breech	2	2.6	0	0.0	0.33	0.56
Oligohydramnios	7	9.3	1	8.3	0.01	0.91
Polyhydramnios	2	2.6	1	8.3	1.00	0.31

**J) Intrapartum Parameters between Monotherapy Group and Polytherapy**

**Table 7:** Comparison chart on intrapartum parameters between monotherapy group and polytherapy

Variable	Monotherapy		Polytherapy		X <sup>2</sup>	P
	N	%	N	%		
Elective CS	7	9.3	2	16.6	0.61	0.43
Emergency CS	24	32	2	16.6	1.86	0.17
Fetal distress	6	8	0	0	1.03	0.30
MSAF	6	8	0	0	1.03	0.30

The frequency of elective LSCS, emergency LSCS, fetal distress and meconium staining studied in the monotherapy/polytherapy groups were comparable

**K) Postpartum Parameters between Monotherapy Group and Polytherapy**

**Table 8:** Comparison chart on postpartum parameters between monotherapy group and polytherapy

Variable	Monotherapy		Polytherapy		X <sup>2</sup>	P
	N	%	N	%		
Infections	5	6.6	1	8.3	0.04	0.83
Seizures	4	5.3	1	8.3	0.17	0.67

The frequency of post partum seizures and infections studied in the monotherapy/polytherapy groups were comparable

## Discussion

In the present study, the WWE on AED were divided into monotherapy and those on polytherapy group and the intake during their periconceptional period was specially considered. It was noted that there were of the WWE on AED, 59.5% were on monotherapy and 9.5% on polytherapy. 31% were not on AED. In my study antenatal seizures were present in 51.7% of women on AEDs.

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. 18.4% had a decrease and 35.6% 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.

All the maternal antenatal complications studied in the monotherapy/polytherapy groups were comparable, this could be due to better antenatal care.

While 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. These were not statistically significant in the monotherapy/polytherapy groups.

Birth weights were comparable in mono/ poly groups. 33.3% of babies in the polytherapy group were LBW but was not statistically significant. Some studies did not show any increase in LBW babies.<sup>7</sup> Birth weight was reduced, though not significant in children of WWE compared with children of healthy women and was pronounced in those who received AED especially polytherapy<sup>8</sup>.

In the present study there was 7.9% birth asphyxia in babies of WWE. There was no statistical

significance in mono/poly groups. 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, but that in the mono/poly group were comparable. This was mainly seen in preterm deliveries.

## Conclusion

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

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