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Foetal outcome and frequency of seizure occurrence in epilepsy complicating pregnancy: a cross-sectional study from Madurai, India.

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Abstract

Background

Epilepsy during pregnancy is a complicated situation for the mother and the baby. It is also a major therapeutic challenge because most of the drugs treating epilepsy have adverse effects on the growing foetus. The main aim of the study was to evaluate the effect of epilepsy on pregnancy, the fetal outcome and frequency of seizure occurrence among pregnant women.

Methods

Epileptic patients admitted in department of Obstetrics and Gynecology (OBG), GRH, Madurai, Tamilnadu, was considered. Detailed obstetric history was recorded. History of seizures (age of onset, type, disease free interval, and history of status epilepticus) were also obtained.

Results

Majority of the epileptic mothers newborns birth weight was between 2.5 -3 kg. followed by 2.49 kg, >3 kg and <2 kg. 94.6% of the babies had good 1 min Apgar score and 93.2% of the babies had good 5 min Apgar score. Increase in frequency of seizures occurrence were observed in 16(21.3%) of cases.

Conclusion

Fetal outcome was relatively good among pregnant epileptic mothers in majority of the cases. Special importance should be given disease free interval and frequency of seizures. Regular intake of antiepileptic drug and more frequent antenatal visits should be continued.

Key words

Apgar score, epilepsy, newborn, pregnancy, seizure.

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Background

Epilepsy during pregnancy is a challenge for the mother and the baby. The maternal trait of epilepsy may predispose neonates to birth defects; recent studies suggest that the risk of birth defects is entirely associated with maternal use of antileptic drugs. Epilepsy complicated pregnancy, is unpredictable with altered seizure frequency in most of the cases [1].

Reports show that high seizure frequency prior to the pregnancy or its duration associated with increased risk during gestation [2]. Some researchers reported, the seizure frequency remains stable in 50% to 85% of pregnancies of epileptic women [3, 4]. A research among 1882 patients revealed that 58.3% remained seizure-free throughout the gestational period. A relatively less population, 2.7% and 3.5%, showed seizures, during delivery [5]. Status epilepticus which is a rare complication involves 1% of pregnancies [6]. In the United States every year more than 25,000 epileptic women deliver viable pregnancies [7]. Seizure rates changes due to discontinuation of oral AED (antiepileptic drug) medication. Sleep deprivation, particularly in idiopathic generalized epilepsies, psychological stress and intermittent, hyperventilation *etc*. [6].

There are explanations for an increase in seizures during pregnancy may be due to lack of proper knowledge because of fear of teratogenic AED effects, enhanced theoretically preconvulsive estrogens, changes in gastric motility, and an increase in nausea and vomiting. Altered pharmacokinetics of AEDs may influence the protein binding or increased hepatic metabolism [8].

Seizure activity during pregnancy increases due to changes in psychological, hormonal and pharmacokinetic activity [9]. Altered the hypothalamo-pituitary-ovarian axis is potential enough to influence reproductive hormone levels. The reason may be due to the involvement of temporal and frontal lobes and hypothalamus responsible for the regulation of reproductive cycle [10]. It is also a major therapeutic challenge because most of the drugs treating epilepsy have adverse effects on the growing foetus. Drug dosage must be balanced based on side effects and seizure frequency [7]. Increased maternal mortality during and soon after pregnancy is also recognized [11]. There are several other complications such as hyperemesis, vaginal bleeding, pre-eclampsia, early and weak contractions, or an increased caesarean section rate occur twice compared with healthy pregnant women [12 - 14].

The main aim of the study was to evaluate the effect of epilepsy on pregnancy, the fetal outcome and frequency of seizure occurrence among pregnant women.

Material and Methods

Study Period

This prospective study was conducted in Government Rajaji Hospital (GRH), Madurai in the period of June 2010 to May 2011.

Study design, participants and the collection of data

All epileptic patients admitted in department of Obstetrics and Gynecology (OBG), GRH, Madurai, Tamilnadu, was considered for this research purpose. At the beginning of the study, detailed history regarding age, booking status, gravida and details of menstrual history, expected date of delivery was enquired. Detailed obstetric history was recorded. History of imminent symptoms like headache, nausea, vomiting, blurring of vision, epigastric pain and oliguria was also noted down. Oligohydramnios, pregnancy induced hypertension (PIH), antepartum hemorrhage, all these types of obstetrical complications were also enquired. Detailed history of seizures (age of onset, type, disease free interval, and history of status epilepticus were also obtained. Pattern of the usage of antiepileptic drugs (type and duration of therapy), intake of AED and folic acid were noted down. Neurological history ruled out central nervous system (CNS) lesion, trauma, infection, and tumor and drug intake pattern. General and systemic examination including thorough CNS examination, per abdominal and per vaginal examination was done for all patients. Blood pressure measured and fundus examination was also done. Neurologist opinion was obtained for all cases.

Hemoglobin (gm%), urine (Alb, sugar) blood urea, sugar, serum creatinine, serum uric acid, serum electrolytes, liver function tests and platelet count were performed. Electroencephalogram (EEG) recording was taken for all the cases. A routine examination like Ultrasonography was done for gestational age assessment, liquor status, intrauterine, growth retardation (IUGR) and to rule out congenital anomalies. All pregnant women were admitted in OBG ward before the expected date of delivery and their epileptic conditions were evaluated and followed up by a neurologist. As these patients gets into labour, they were monitored carefully with partogram and mode of delivery was recorded.

Caesarean section was done for obstetric indications. Evaluation of maternal outcome was done by occurrence of seizures during labour or postpartum carefully observed. Complications like oligohydramnios, pregnancy induced hypertension (PIH), antepartum haemorrhage, postpartum haemorrhage was also carefully monitored. Foetal outcome was obtained by the Birth weight of the baby, Apgar (appearance, pulse, grimace, activity, respiration) scoring and evidence of any congenital anomalies. Apgar scoring was

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recorded for 1 and 5 minutes. Paediatric opinion was obtained for all neonates.
Premature neonates, low Apgar scores, IUGR and birth anomalies were admitted immediately in neonatal intensive care units (ICU)s. Head circumference measurement was done for all babies. All delivered epileptic patients were observed in the labour ward for period of 48 hours following delivery. Computed tomography (CT) scan was performed and AEDs were continued postnatally among all patients. Neurologist advice was taken before discharge the patient. Postnatal counseling also done to continue the AEDs.

Inclusion criteria

All pregnant women with history of epilepsy were considered for this study. Both primigravida and multigravida, booked and unbooked cases were included. All type of seizure disorders, generalized tonic-clonic seizures (GTCS, Partial) regular or irregular intake of AEDs, (monotherapy or polytherapy), patients not on AEDs as per neurologist advice, patients who discontinued AEDs by themselves.

Exclusion criteria

Eclamptic patients, postpartum seizure (including Eclampsia, cases of metabolic encephalopathy/drug toxicity, psychogenic causes were set up as exclusion criteria for this research. There were some other medical conditions like diabetes mellitus, hypertension, tuberculosis, heart disease and renal disease were excluded.

Ethical committee approval

Permission from Ethical Committee of the hospital was obtained for research purpose. The present research was done according to the declaration of Helsinki (Latest version). Consent was also taken individually from the participants.

Outcome variable

Socio demographic details, age was considered as outcome variable.

Explanatory variables

Apgar score, frequency of seizures, disease free interval was set up as Explanatory variables.

Data management and statistical analysis

A master chart was prepared to enter the collected data. To obtain the association between different variables, statistical analysis (Chi-square test) was done by using Epidemiological Information Package (Epi Info™ 2010) developed by Centre for Disease Control and Prevention, Atlanta, GA 30333. A 'p' value less than 0.05 was considered statistically significant.

Results

Babies average head circumference was 33.5cms, with range of 30-35cms which was within normal limits.

Table 1 – Frequency of birth weight of newborn n(%)

Birth weight (kg)	Cases
< 2 kg	4(5.3)
2 - 2.49 kg	13(17)
2.5 – 3 kg	49(66)
> 3 kg	9(12)
Total	75(100)
Low birth weight	17(22.3)
Term low birth weight	6(9.3)
Range	1.1 – 3.8 kg
mean±SD	2.65±0.44

Table 1 clarifies frequency of birth weight of newborn. Majority of the epileptic mothers newborns birth weight was between 2.5 -3 kg. followed by 2.49 kg, >3 kg and <2 kg.

Table 2 – Apgar score n(%)

Apgar Score	At 1 minute	At 5 minutes
2	2(2.7)	-
3	1(1.4)	-
4	1(1.4)	1 (1.4)
5	-	1(1.4)
6	70(94.6)	2(2.7)
7	-	1(1.4)
8	-	69(93.2)
Total	74(100)	74(100)
Range	2-6	4-8
Mean±SD	5.82±0.77	7.84±0.66

Table 2 explains 94.6% of the babies had good 1 min Apgar score and 93.2% of the babies had good 5 min Apgar score.

Table 3 – Frequency of seizures among epileptic mothers n(%)

Frequency of seizures	Cases
Increased	16(21.3)
Not increased	59(78.7)
Total	75(100)

Increase in frequency of seizures occurrence were observed in 16(21.3%) of cases (Table 3).

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Table 4 – Relationship between disease free interval and obstetric complications n(%)

Disease free interval	Obstetric complications	
	Present	Absent
0-1 years	7(33.3)	14(66.7)
>1 year	14(25.9)	40(74.1)
Mean±SD	5.77±4.4	4.84±3.92 years
P value	0.391[x]	

[x]P>0.05 statistically not significant

Table 4 shows the relationship between disease free interval and obstetric complications. Majority of the cases of 0-1 years of disease free interval, obstetric complications were absent, in case of >1 years, 74.1% of cases complications were absent. There is no statistically significant correlation between the disease free interval and occurrence of obstetric complications was found.

Table 5 – Relationship between disease free interval and frequency of seizures n(%)

Disease free interval	Frequency of seizures	
	Increased	Not increased
0-1 years	16(76.2)	5(23.8)
>1 year	-	54(100)
Mean±SD	0.29±0.27	6.41±3.57
P value	0.0001[†]	

[†]P<0.05 statistically significant

Table 5 explains there was increased seizure frequency in 76.2% of cases with disease free interval of less than one year and there was no increase in seizure occurrence in which the disease free interval is more than one year. Statistically significant correlation observed between the disease free interval and frequency of seizures.

Discussion

Epilepsy in pregnancy is a critical situation for the mother and the baby, also a challenge to the doctors. The setting of the present research provided us a unique opportunity to evaluate fetal outcome and seizure frequency among pregnant women.

Birth weight of newborn of epileptic mothers

According to the review of literature pregnant epileptic patients have several complications like increased frequency and aggravation of seizures, obstetric risks with adverse neonatal outcome compared to general population. In this study the birth weight of neonates range from 1.1 -3.8 kg with mean birth weight of 2.65 kg. 5.5% of our babies had birth asphyxia (Apgar 1'= 2-6, 5'= 3-7). In Thomas *et al*, study the birth weight ranges from 1.8- 4.0 kg with mean weight of 2.84 kg. 10.7% of babies had birth asphyxia (Apgar 1' = 2-6,5'= 3-7) [15]. Birth weight of less than 2.5 kg accounted for 22.3% in this study. Similarly Chattopadhyay *et al*, has reported 23.3% and Goel *et al*, has reported 18% of low birth weight babies [16, 17]. Thomas *et al*, has reported 21% of term low birth weight babies. In this study term low birth weight constitute only 9.3%.

Head circumference of the newborns

Average head circumference was 33.5 cms, with range of 30-35cms which was within normal limits in this study. It was similar to Thomas *et al* study where there was average head circumference of 35 cms, with range of 32- 44cms [18].

There were no cases of microcephaly in this study. Except for one foetus with congenital diaphragmatic hernia, whose mother was on phenytoin, there was no other congenital anomalies like neural tube, craniofacial, digital, cardiac, urogenital defects in fetuses. This finding is dissimilar with others, where 2-3 fold increase in major congenital malformations (MCM) in babies of WWE treated with a single AED during pregnancy was mentioned [19]. Thomas has mentioned that GIT anomalies like esophageal atresia, omphalocele, hernia (diaphragmatic, inguinal and umbilical) can occur in women with AED [15].

Frequency of seizures

In our study we observed that there was increased seizure frequency in 76.2% of cases with disease free interval. Other researchers showed the seizure frequency was decreased in 13% cases and 68% pregnancies, increase was associated with non-compliance with the drug regimen or disturbed sleep pattern [20]. Some studies reported the increase in seizure activity was in last trimester of pregnancy [21].

Conclusion

From the present study, it can be concluded that the fetal outcome was relatively good among pregnant epileptic mothers in majority of the cases. This also indicates more awareness amongst the patients reflected in early booking, regular antenatal care, regular intake of anti epileptic drugs, folic acid etc. Special importance should be given disease free interval and frequency of seizures, as one fifth of our cases significantly correlating the conditions, shorter the disease interval higher the incidence of seizure frequency. Regular intake of antiepileptic drug and more frequent antenatal visits should be continued. Genetic counseling may be helpful in this context, if the disease is inherited. Close contacts between neurologist, obstetrician and the pediatrician is strongly recommended in epilepsy complicating pregnancy.

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Limitations & future scope of the study

The present study is a cross-sectional study with limited sample size. Future researches should include all the hospitals in the state to give a better scenario.

Abbreviations

AED (antiepileptic drug), Antiepileptic drugs (AED), Central nervous system (CNS), CNS (central nervous system), Computed tomography (CT), Electroencephalogram (EEG), Government Rajaji Hospital (GRH), Generalized Tonic-Clonic Seizures (GTCS), Intrauterine, growth retardation (IUGR), Neonatal intensive care units (ICU)s, Obstetrics and Gynecology (OBG), pregnancy induced hypertension (PIH).

Competing interests

Authors declare that they do not have any competing interest.

Authors' contribution

Dr. Indumathi Sivaji and Dr. Jeyarani Pitchah designed the study, conducted the research, analyzed, interpreted the data, drafted the manuscript, and revised it. All authors took part in critical revision and finally approved the manuscript for publication.

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