

TO STUDY FETOMATERNAL OUTCOME IN PREGNANT WOMEN WITH EPILEPSY

Obstetrics & Gynaecology

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ABSTRACT

Introduction: Epilepsy is a common neurological disorder in obstetrical practice. Around 20 million women all around the world suffer from epilepsy (WHO data). In India, about 2.7 million women in India suffer from epilepsy, with 52% of them being in the reproductive age group. **Methods:** 50 pregnant women with epilepsy admitted to the labor room/ward of the Department of Obstetrics and Gynecology of Pt. B.D. Sharma Post Graduate Institute of Medical Sciences Rohtak. A prospective observational study was done and various fetomaternal outcomes were studied. Maternal outcome variables studied were onset of labor (term, preterm), development of pre-eclampsia and abruptio placentae, type of labor (spontaneous or induced), mode of delivery, PPH, ICU admissions. Fetal outcome variables included pre-maturity, Apgar score, birth weight, fetal growth restrictions and presence of gross congenital malformations. Results obtained were analyzed by descriptive measures in terms of frequency and percentages. **Results:** There was an equal number of patients who had a seizure in the current pregnancy and who did not have a seizure in the current pregnancy. Most of them had it in the 2nd and 3rd trimester. 40% of the patients had anemia. Most of the patients had no abnormalities in EEG (84%) and MRI (90%). 88% of patients were on monotherapy. The. Most of the patients delivered at term (70%). There were 2 patients with pre-eclampsia and one patient each with IUGR and twins. 28% of the patients needed induction of labor. 18% of the patients delivered by lower segment cesarean section. Status epilepticus was an indication of LSCS in 1 patient. ICU admission was needed in 2 patients (4%). There were no maternal mortalities in this study. Apart from one neonate all neonates had a high Apgar score. There was one case of cleft lip and one neonate with cleft lip + palate. The majority of the neonates 89.79% (44/49) did not require NICU admission. There were two IUGRs. There was one neonatal death due to prematurity. **Conclusion:** Pregnant women with epilepsy require meticulous care during pregnancy. Most of these patients had favorable maternal and fetal outcomes in well controlled epilepsy with single antiepileptic drug.

KEYWORDS

INTRODUCTION

A seizure is defined as involuntary neuromuscular activity which may involve localized parts of the body or involving the entire body. They may be classified as generalised tonic clonic type, focal partial seizure, absence seizures and myoclonic jerks [1] The incidence of acute symptomatic seizures is around 29–39 per 100,000 per year. [2] In India, about 2.7 million women in India suffer from epilepsy, with 52% of them being in the reproductive age group. [3, 4] In India, the number of women with epilepsy is estimated to be around 2.73 million, with 52% of these being in the reproductive age group.

The uniqueness of pregnancy is in the fact that the physiological changes of pregnancy can change the course of the disease and also alter the pharmacokinetics of the ingested medications, rendering the therapy more complicated. The adverse effects of the anti-epileptic drugs needs to be weighed against the advantages of prevention of seizure in pregnancy, thereby posing unique challenges to the patient and the treating physician.

The various changes that occur during pregnancy which can alter seizure frequency. These include hormonal variations, changes in drug absorption / distribution/ excretion, psychosocial adjustments including social stresses, sleep deprivation and adherence to anti-epileptic drugs. [5] Hormonal changes during pregnancy may have an effect on the outcomes in pregnancy [6]

Pregnant women with epilepsy have an otherwise uncomplicated course commonly. However, the condition may complicate the course of pregnancy. Some women with epilepsy may have increased chances of spontaneous miscarriage, antepartum haemorrhage, hypertensive disorders, etc and hence, are high-risk pregnancies. Seizure frequency during pregnancy will remain unchanged in ~50% of women, increase in ~30%, and decrease in ~20%. [7]

Seizure control during pregnancy is the most important step to reduce risk of adverse pregnancy outcomes. [8] Women with epilepsy have an increased risk of fetal malformations. Overall, it is preferable to use the least number of medications, for the least frequency at the least dosage to reduce the maternal and fetal side-effects of anticonvulsant medications. [9]

Many studies have been done to evaluate the fetomaternal outcomes in pregnant women with epilepsy in different parts of the world. In India, very few studies have been conducted on the topic [10,11] There are still many lacunae in the optimal management of pregnant women with epilepsy, which is one of the reasons of taking up this study. [12] This prospective observational study was conducted to evaluate pregnant women with epilepsy and its impact on maternal and fetal outcome.

MATERIALS AND METHODS

This was a 1.5 year (January 2021 to June 2022) prospective observational study conducted in the department of OBGYN in a tertiary care teaching hospital in Northern India after IEC clearance. Informed and written consent was obtained from all patients. Pregnant women (after gestational age of 28 weeks) with epilepsy admitted to the labour ward and undergoing completion of pregnancy here were included. Those with eclampsia, metabolic encephalopathy and known major psychiatric illnesses were excluded. Sample size was estimated to be 50 based on prior existing literature [13] Detailed history including past history regarding onset of epilepsy, duration of epilepsy, type of seizure/epilepsy, controlled/uncontrolled, number of anti-epileptic drugs (AEDs), compliance towards treatment and treatment history was taken from the patient.

History of presenting complaints was recorded in detail from each patient. General physical, systemic and obstetric examination and neurological examination was carried out. Routine antenatal investigations and necessary neurological investigations including EEG, MRI Brain (if required), and ultrasonography for fetal well-being was done. Maternal outcome variables to be studied were onset of labor (term, preterm), development of pre-eclampsia and abruptio placentae, type of labor (spontaneous or induced), mode of delivery, PPH, ICU admissions. Fetal outcome variables included pre-maturity, Apgar score, birth weight, fetal growth restrictions and presence of gross congenital malformations.

Statistical Methods

Descriptive measures were analyzed by using mean and standard deviation and Student t-test was applied and proportion were analyzed by applying Chi-square test. Statistical analysis was performed by using Microsoft Excel StatPac V365.

RESULTS

The age distribution of the patients is shown in table 1. Majority (90%) of the patients belong to the 21-30 years age group. There were very few patients in the 31-40 years age group (10%) and even lesser in the <20 years (4%). The mean age was 26.36 +/- 3.53 years, minimum being 19 years and maximum being 34 years. 62% were from a rural setting and the remaining were from an urban setting (38%). Most of the patients belonged to the lower middle class (46%) and upper lower class (30%). Only 6% belonged to the upper middle class. Most of the patients were housewives (86%) and the remaining 14% were employed. Second gravida constituted the highest group (38%), which was closely followed by primigravida (32%) and G3 or more (30%).

As shown in table 2, there was an equal distribution of patients who had a seizure in the current pregnancy and did not have a seizure in the current pregnancy. Among those who did not have a seizure in the current pregnancy, majority of the patients (56%) had a seizure more than 2 years prior. Very few patients (8%) had a seizure within 1 year time. Among those who had seizures in the current pregnancy, most of them had it in the 2nd trimester or 3rd trimester. Very few (12%) had it in the first trimester. There were 4 patients who had a seizure in the recent past (<1 week prior to presentation).

With respect to duration of epilepsy, majority (27 patients - 54%) had a duration of epilepsy above 5 years duration. 18% of patients each had a duration of 3 years and 5 years respectively. Remaining (14 patients - 28%) had a duration of epilepsy < 3 years.

The average gestational age at delivery was 37.4 weeks. Majority delivered at term (35 patients - 70%). The proportion of patients who delivered between 34-37 weeks was 38% (9 patients). 12% of the patients delivered between 28-34 weeks of gestation. (figure 1)

Maternal Outcomes

There were 2 patients with preeclampsia (4%) and one patient each with IUGR (2%) and twins (2%). With respect to onset of labour, 72% (36 patients) had spontaneous onset of labour while 28% of the patients needed induction of labour. With respect to mode of delivery, 82% (41 patients) had vaginal delivery while 18% (9 patients) delivered by lower segment cesarean section. Out of the 9 LSCS, 6 were for fetal distress, 1 was for previous 2 LSCS and 1 was for breech presentation. One was for status epilepticus.

Maternal Complications.

One patient needed medical management of PPH. Majority of the patients (96%) did not require ICU admission. Only 2 (4%) needed ICU admission (one of which was due to PPH, other was due to status epilepticus). There were no maternal mortalities in this study group. Prevalence of anemia (Number of patients with anemia (Hb <11) was 40% (20 patients). None of the patients had severe anemia. 14% of the patients had deranged liver function tests. Most of these were among those who were on polytherapy. Most of the patients (84%, 42 patients) had a normal EEG waveform and one patient had increased discharge in temporal electrodes. EEG was not done in 7 patients (14%). MRI was done in 46 of the 50 patients in the study, and majority 45 patients (90%) was normal. Only one patient showed increased T2 signal in white matter, with no focal lesions. Majority of the patients (88%) were on monotherapy. (table 3)

Neonatal Outcomes.

There was one pair of twins in this study. There 48 live births and 2 intrauterine fetal demises. There was one neonatal death due to severe preterm delivery. This is one of the twins. Most of the neonates (37%) had a weight more than 3kg. There were 10 neonates weighing less than 2 kg (Figure 2). The average birth weight was 2.79 kg. Apart from one neonate having an Apgar score of 5/10 at the 1st minute and one other neonate having an Apgar score of 7/10 in the 5th minute, all neonates had an Apgar score of 9/10. There was one case of cleft lip and one neonate with cleft lip + palate. There were no malformations in 49/51 neonates. Majority of the neonates 89.79% (44/49) did not require NICU admission.

DISCUSSION

In this study, we have analyzed 50 patients with epilepsy in pregnancy, as described in the methodology.

Age

In the present study, the age distribution was as follows. The proportion

of age <20 years (4%) and age 31-40 years (10%). This is similar to the proportional distribution of age groups in the study by Malik et al. In their study, the proportion of patients in the age group <20 years was 9% and the proportion of patients in the age group >31 years was 9%. This finding is also similar to the findings of the study by Arti Sharma et al [14], wherein the proportion of patients in the age group <21 years was 13% and the proportion of patients in the age group <31 years was 9.3 years.

Duration Of Epilepsy

In our study, the proportion of patients with duration of < 3 years was 28%, proportion of patients with duration of epilepsy between 3-5 years was 18% and proportion of patients with duration of epilepsy >5 years was 54%. This is slightly different from the observations of Raji et al. In their study, the proportion of patients with duration of epilepsy < 1 year was only 7.27%. The proportion of patients with duration of epilepsy between 1-5 years was 30%. The proportion of patients with a duration of epilepsy of more than 5 years was 49%, which was comparable to the findings of our study.

Occurrence Of Seizure During Pregnancy

In our study, 50% of the patients (25/50) had seizures in the current pregnancy. This is similar to the findings of Thomas et al (53%) and Bansal et al (53.7%) rates of recurrence. In the study by Sharma SR et al, out of the patients who had been diagnosed of epilepsy prior to pregnancy itself, 79% remained seizure free and 21% had seizures during the index pregnancy. In the study by Raji et al, out of 110 patients who had been diagnosed of epilepsy prior to pregnancy itself, 13.63% (15/110) patients developed seizure during the index pregnancy.

Monotherapy Vs Polytherapy

In our study, it is of important significance that most of our patients were on monotherapy (88%). In most of the comparable studies (shown in table), the proportion of patients who were on monotherapy was much lesser (Raji et al - 53%, Sharma et al 45%, Thomas et al - 60%, Bansal et al (older cohort-59%, newer cohort -69.4%). The problems associated with polytherapy are much higher than that of monotherapy. Apart from those few patients who do not respond adequately to monotherapy, it is best to avoid polytherapy. [1]

Gestational Age At Delivery

In the present study, the average gestational age at delivery was 37.4 weeks and the proportion of patients who delivered preterm was 30%. In the study by Sharma SR et al, [12] the average gestational age was 37 weeks. In the study by Raji C et al [49], the proportion of patients with prematurity was only 11.4%. In the study by Thomas et al, the propensity of epileptic patients going into preterm labour was surprisingly lesser than a control population (3.8% vs 6.1%, p value<0.001). In the study by Borthen et al [17], epileptic patients on optimal treatment did not have a propensity for preterm labour, but those who were not on treatment had a higher frequency of preterm labour.

Mode Of Delivery

In our study, there was an 18% LSCS rate. The proportion of cesarean section in the study by Raji et al was 28%. Thomas et al note a 30% rate of cesarean section among those mothers with epilepsy. In the study by Bansal et al, the CS rate in the older cohort was 25.4% and that in the newer cohort was 26.8%. In the study by Malik et al [47], the Cesarean section rate was 29%. Overall, compared to a general population, there seems to be a higher risk of cesarean section among women with epilepsy. In the study by Borthen et al [23], the odds ratio of cesarean section among women with epilepsy compared to those without epilepsy was 2.5. In the large meta-analysis by Razzaz et al, [18] the adjust relative risk for cesarean section was 1.58.

Birthweight

In our study, the average birth weight was 2.79 kg. This is comparable to the findings of the study by Bansal et al wherein the average +/-SD was 2757 +/-441 grams in the older cohort and 2823 +/-563 grams in the newer cohort. This average weight is slightly higher than the findings of Thomas et al, wherein the average weight was 2.46 +/- 1.1 kg. The distribution of weight in our study is similar to that of findings by Malik et al and Raji et al. Overall, in the large meta-analysis by Razzaz et al, [18] it has been stated that the odds ratio of a small-for-gestational age at birth is around 1.25. Pennell et al [19] showed that there was 12.9% increase in the risk of small-for-gestational age at birth.

Fetal Loss (IUFD/Stillbirth/ Neonatal Death)

In our study there were very few 2 intrauterine fetal demises and 1 neonatal death. Overall, this is comparable to the studies by Bansal et al and Sharma et al. In the study by Bansal et al, there were no stillbirths in the older cohort. There was one stillbirth in the newer cohort (1/219). In the study by Sharma et al, there were no stillbirths in the group receiving Levetiracetam monotherapy and there was one stillbirth in the group receiving levetiracetam polytherapy (1/56). Studies by other authors have suggested higher rates of fetal loss. In the study by Raji et al [47], the proportion of stillbirths was 8.57% (9/105). In the study by Razzaz et al (large meta-analysis, [18] the odds ratio for having stillbirth is suggested to be 1.55.

Malformations

In our study, the only malformations noted were cleft lip and cleft lip+palate. This is similar to the study by Raji et al, wherein 110 epilepsy cases and there was one neonate with cleft lip and cleft palate, yielding a congenital anomaly rate of only 0.9%. The Eurocat registry showed an increase of malformations like neural tube defects and cleft palate and other problems [20,21] Rezaallah suggest that communication of risks about anti-epileptic drugs should be given more importance. [22] Güveli et al suggest that the bulk of the teratogenicity is due to valproate, and this drug should be best avoided. [23]

CONCLUSIONS

Epilepsy in pregnancy, though rare, requires meticulous care during pregnancy. Most of the patients deliver at term gestation. Preterm delivery is not a major problem. Interventions such as induction of labour and cesarean section are needed in a small group of these patients. Overall, neonatal outcomes are excellent in this group of patients with epilepsy in pregnancy. Overall, there seem to be no major risks for women with epilepsy during pregnancy, provided they are compliant to medications and regular in follow-up.

Clinical Significance

This finding of the present study can help in guiding the obstetrician handling a case of epilepsy in pregnancy, in terms of management, decision-making and counselling aspects.

Table 1. Age and parity distribution

Age distribution	Age group	Number of patients	Percentage
	<20 years	2	4%
	21-30 years	45	90%
	31-40 years	5	10%
Parity distribution	Parity group	Number	Percentage
	Primigravida	16	32%
	G2	19	38%
	G3 or more	15	30%

Table 2. Presentation of seizure in relation to pregnancy

Patients who did not have a seizure in the current pregnancy		N=25	Percentage
Time elapsed since last seizure	< 1 year duration	2	8%
	1 year	11	36%
	2 years	12	56%
Number of patients who had a seizure in the current pregnancy		N = 25	Percentage
Trimester of presentation	1st trimester	4	12%
	2nd trimester	11	44%
	3rd trimester	10	40%

Table 3. Type of therapy

Type of medication	Number	Percentage
Monotherapy	44	88%
Polytherapy	6	12%
Total	50	100%

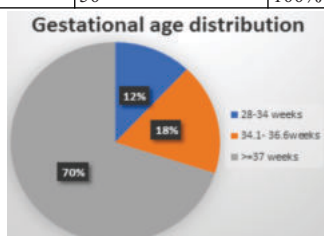


Figure 1. Gestational age distribution

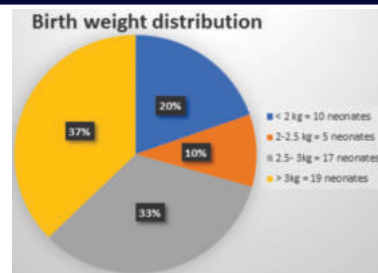


Figure 2. Birthweight Distribution

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