



RESEARCH ARTICLE

FETOMATERNAL OUTCOME IN EPILEPSY IN PREGNANCY IN A TERTIARY CARE HOSPITAL

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Abstract

Background: Epilepsy is the most commonly encountered neurological disorder in Obstetrics after migraine. Incidence of seizure disorder in pregnancy is estimated to be 0.3 - 0.5% of all births. Infants born to mothers with epilepsy and exposed to antiepileptic drugs (AEDs) in utero have increased risk for birth defects (4–6%) when compared with infants not exposed (1–2%) to these drugs.

Objective: To assess the fetomaternal outcome in pregnancy with epilepsy in Jammu.

Methods: This prospective study was conducted over a period of one year in the Department of Obstetrics and Gynecology, SMGS Hospital, a tertiary care center, Jammu, India. Total 130 epilepsy cases were included in this study. These patients were managed with a team of neurologist, obstetrician, radiologist and a neonatologist. The patients were thoroughly examined, assessed and monitored regarding the fetomaternal outcome.

Results: In our study, we have included 130 epilepsy patients. The incidence of epilepsy in pregnancy in our hospital is 0.54%. The mean age of participating women in our study was 24.7±8.63 years. 41 (31.5%) were using Lamotrigine as antiepileptic drug in pregnancy, gestational hypertension was the most common maternal complication in 28 (21.5%). Mode of delivery was LSCS in majority of the women i.e. 74 (56.9%).

Conclusion: These women should be managed with monotherapy at the lowest possible dosage to diminish the risk of complications and also maintain good seizure control. The perinatal complications can be diminished by the close coordination between the Neurologists, Obstetrician and the Pediatrician.

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Introduction:-

Epilepsy is the most commonly encountered neurological disorder in Obstetrics after migraine. Incidence of seizure disorder in pregnancy is estimated to be 0.3 - 0.5% of all births¹. Pregnancy with epilepsy is considered high risk mainly due to teratogenic potential of antiepileptic drugs and increased risk of pregnancy and neonatal complications like hypertension, preeclampsia, antepartum hemorrhage, caesarean delivery, still births, neonatal

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deaths, intrauterine growth restriction and preterm delivery. However, several studies have also been published that no significant increase in these complications in pregnancy with epilepsy^{2,3,4}.

Infants born to mothers with epilepsy and exposed to antiepileptic drugs (AEDs) in utero have increased risk for birth defects (4–6%) when compared with infants not exposed (1–2%) to these drugs⁵⁻¹³. Unfavorable neurologic and cognitive long-term development also recently was reported to be more frequent in children born to mothers with epilepsy than in controls, in spite of the great individual variation¹⁴⁻¹⁶, and recent studies suggested that school-aged children of mothers with epilepsy have more additional educational needs than do controls¹⁷. However, many factors other than AED exposure may contribute to the observed neurodevelopmental, cognitive, and psychosocial problems in these children. These confounding factors include, for example, seizures during pregnancy, the seizure/epilepsy/epilepsy syndrome type of the mother, genetic factors, maternal age/parity, mother's cognitive functioning, and socioeconomic status^{10,18}.

Although guidelines on the management of pregnant women with epilepsy have been published for neurologists^{13,15}, recent reports from the United States and the United Kingdom suggest that antenatal care offered to women with epilepsy does not follow currently recommended optimal care practices^{17,18}.

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 population¹⁹⁻²¹. Frequency of seizures is increased during pregnancy in one-third of women with epilepsy^{19,22}.

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^{21,23}.

Objective:-

To assess the fetomaternal outcome in pregnancy with epilepsy in Jammu.

Methodology:-

This prospective study was conducted over a period of one year in the Department of Obstetrics and Gynecology, SMGS Hospital, a tertiary care center, Jammu, India. Total 130 epilepsy cases were included in this study. These patients were managed with a team of neurologist, obstetrician, radiologist and a neonatologist. 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 alpha-fetoprotein 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.

Maternal variables analysed were age, parity, duration of epilepsy, seizure during pregnancy, antiepileptic drug usage in pregnancy, maternal complications and mode of delivery. Fetal outcome variables observed were number of live birth, still birth, birth weight, Apgar score, observation of congenital anomalies and other perinatal complications. Maternal and fetal outcome variables were presented as frequencies and percentages.

Statistical Analysis:

The recorded data was compiled and entered in a spreadsheet (Microsoft Excel) and then exported to data editor of SPSS Version 20.0 (SPSS Inc., Chicago, Illinois, USA). Continuous variables were expressed as Mean±SD and categorical variables were summarized as frequencies and percentages. Graphically the data was presented by bar and pie diagrams.

Results:-

In our study, we have included 130 epilepsy patients. The incidence of epilepsy in pregnancy in our hospital is 0.54%.

Table 1:- Age (years), parity and duration of epilepsy.

Age (Years)	Frequency	Percentage
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Age (Years)	≤ 20	11	8.5
	21-25	68	52.3
	26-30	25	19.2
	31-35	21	16.2
	> 35	5	3.8
Parity	P0	67	51.5
	P1	31	23.8
	P2	18	13.8
	P3	6	4.6
	≥P4	8	6.2
Duration of epilepsy (Years)	< 1 Year	12	9.2
	1-5 Years	45	34.6
	6-10 Years	27	20.8
	11-15 Years	24	18.5
	> 15 Years	22	16.9

Mean Age±SD=24.7±8.63:

In our study patients, majority i.e. 68 (52.3%) aged between 21-25 years followed by 25 (19.2%) women who were aged 26-30 years, 21 (16.2%) patients belonged to age group of 31-35 years, 11 (8.5%) women were <20 years of age while as only 5 (3.8%) women aged >35 years. The mean age of participating women in our study was 24.7±8.63 years. Out of 130 women, 67 (51.5%) patients were primipara, 31 (23.8%) patients were para 1, 18 (13.8%) patients were para 2, 6 (4.6%) women were para 3, whereas 8 (6.2%) women were more than equal to Para 4. Duration of epilepsy was 1-5 years in majority of participating women i.e. 45 (34.6%), 27 (20.8%) women had epilepsy for 6-10 years, 24 (18.5%) women had epilepsy from 11-15 years. Duration of epilepsy was >15 years in 22 (16.9%) women whereas 12 (9.2%) women had epilepsy since <1 year.

Table 2:- Antiepileptic drugs in pregnancy.

Drug	Frequency	Percentage
Lamotrigine	41	31.5
Carbamazepine	14	10.8
Levetiracetam	11	8.5
Lamotrigine+clobazam	11	8.5
Carbamazepine+clobazam	9	6.9
Sodium valproate	8	6.2
Phenytoin+clobazam	6	4.6
Phenytoin sodium	5	3.8
Sodium valproate+Clobazam	3	2.3
Sodium valproate+Levodopa	2	1.5
No treatment	20	15.4
Total	130	100

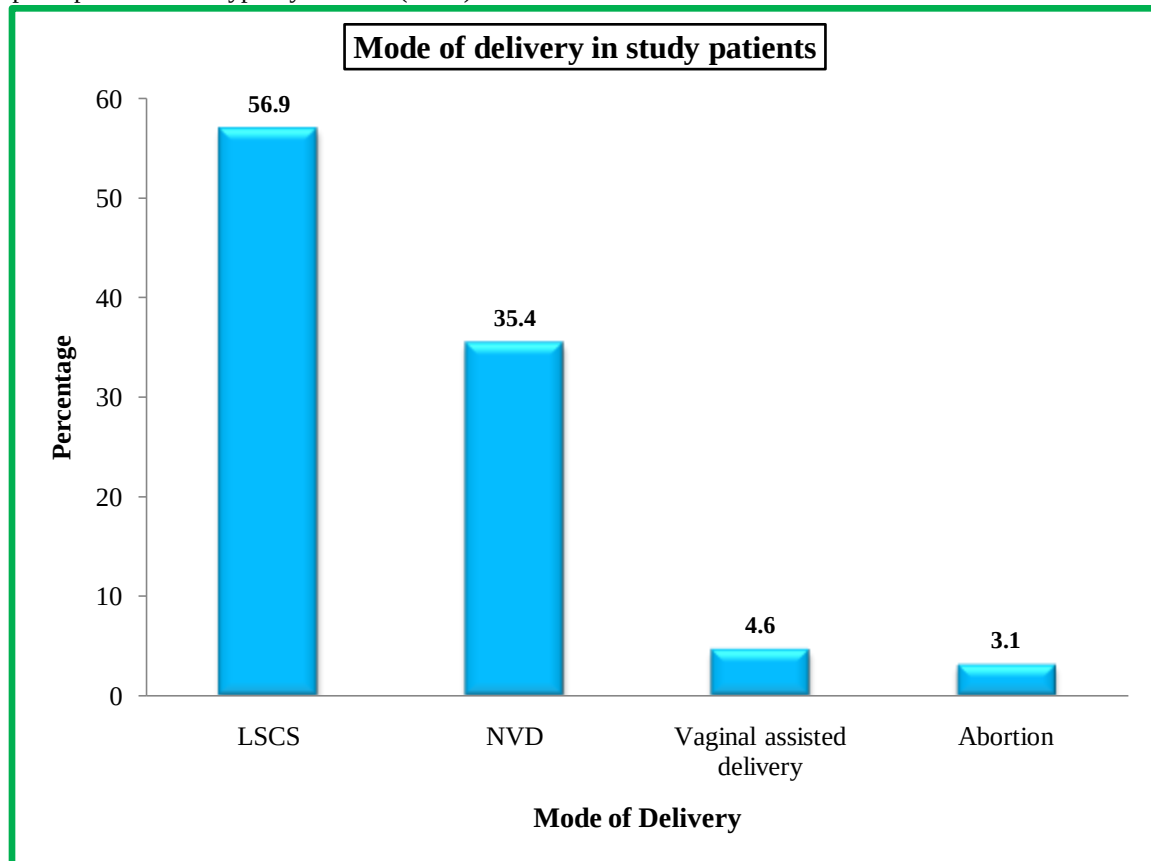
Out of 130 studied women, 41 (31.5%) were using Lamotrigine as antiepileptic drug in pregnancy, 14 (10.8%) were using Carbamazepine, 11 (8.5%) each were using Levetiracetam and Levetiracetam + clobazam combination, 9 (6.9%) women were using Carbamazepine+clobazam. 8 (6.2%) women used sodium valproate, 6 (4.6%) used phenytoin+clobazam, 5 (3.8%) used phenytoin sodium, 3 (2.4%) were having Sodium valproate+clobazam, 2 (1.5%) women used Sodium valproate+Levodopa. 20 (15.4%) women were not on epileptic treatment.

Table 3:- Maternal complications in study patients.

Maternal Complications	Frequency	Percentage
Gestational hypertension	28	21.5
PROM	10	7.7
GDM	5	3.8
Abruption placenta	4	3.1
Hypothyroid	4	3.1

Total	51	39.2
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Maternal complications included gestational hypertension in 28 (21.5%), PROM in 10 (7.7%), GDM in 5 (3.8%), Abruptio placenta and hypothyroid in 4 (3.1%) women each.



Mode of delivery was LSCS in majority of the women i.e. 74 (56.9%), followed by normal vaginal delivery in 46 (35.4%), 6 (4.6%) had vaginal assisted delivery and 4 (3.1%) had abortion.

Table 4:- Fetal outcome and birth weight in study neonates.

		Frequency	Percentage
Fetal outcome	Live birth	120	92.3
	Still birth	10	7.7
	Total	130	100
Birth weight (kgs)	< 2 Kg	11	8.5
	2-2.4 Kg	14	10.8
	2.5-3 Kg	82	63.1
Birth weight (kgs)	> 3 Kg	23	17.7
	Total	130	100
	Mean±SD=2.74±0.93		

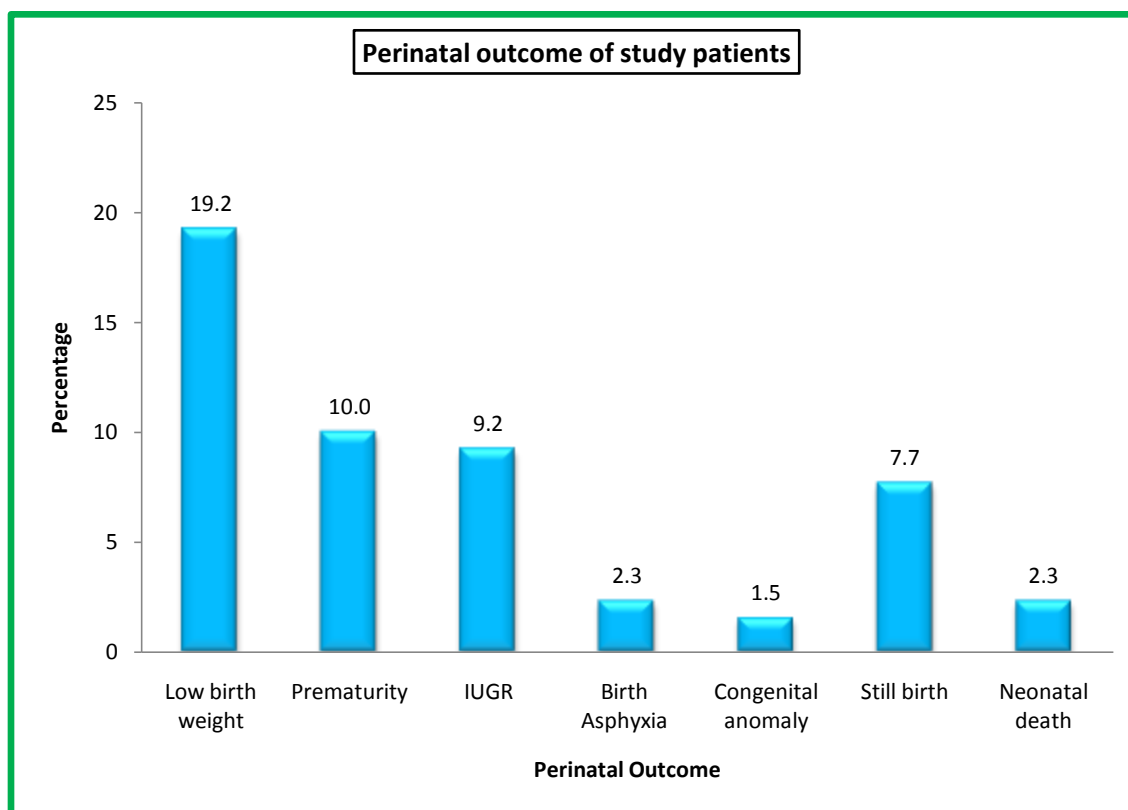
There were 120 (92.3%) live births and 10 (7.7%) still births in our study. Birth weight was 2.5-3kgs in majority of neonates i.e. 82 (63.1%) followed by >3kg in 23 (17.7%) neonates. 14 (10.8%) neonates had 2-2.4kg weight whereas 11 (8.5%) neonates weighed <2kg.

Table 5:- Apgar score.

Apgar Score	Mean	SD
1 Minute	7.62	1.21

5 Minute	9.37	1.65
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Mean apgar score at 1 minute was 7.62+1.21 and at 5 minutes it was 9.37+1.65.



There were 25 (19.2%) low birth weight neonates followed by 13 (10.0%) premature. IUGR was seen in 12 (9.2%) neonates, still birth in 10 (7.7%) neonates, 3 (2.3%) neonates had birth asphyxia, 3 (2.3%) expired. Only 2 (1.5%) neonates had congenital anomaly.

Table 6:- Maternal mortality in study patients.

Maternal Mortality	Frequency	Percentage
Yes	2	1.5
No	128	98.5
Total	130	100

In our study of 130 patients only 2 (1.5%) was the maternal mortality. Out of the expired 2 mothers, one died due to meningioma brain and the other due to cardiac arrest (case of epilepsy with severe anemia leading to cardiac failure).

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^{22,24}. 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^{19,20,25}.

In our study, we have included 130 epilepsy patients and the incidence of epilepsy in pregnancy in our hospital is 0.54%. Incidence of seizure disorder in pregnancy is estimated to be 0.3 - 0.5% of all births¹.

In our study patients, majority i.e. 68 (52.3%) aged between 21-25 years followed by 25 (19.2%) women who were aged 26-30 years with a mean age of 24.7±8.63 years. Out of 130 women, 67 (51.5%) patients were primipara, 31 (23.8%) patients were para 1, 18 (13.8%) patients were para 2, 6 (4.6%) women were para 3, whereas 8 (6.2%) women were more than equal to Para 4. Duration of epilepsy was 1-5 years in majority of participating women i.e. 45 (34.6%), 27 (20.8%) women had epilepsy for 6-10 years, 24 (18.5%) women had epilepsy from 11-15 years. Duration of epilepsy was >15 years in 22 (16.9%) women whereas 12 (9.2%) women had epilepsy since <1 year. Similar results were obtained by Raji C et al. (2017)²⁶ in a study to evaluate fetomaternal outcome in patients with epilepsy. In their study maximum number of cases 53 (48.18%) were in the age group between 21-25 years with most 58 (52.73%) primigravida women. In their study most 68 (61.82%) women had epilepsy of more than 5 years. 15 patients had seizure during pregnancy. Of which 2 had new onset seizures. Among 110 patients, 15 patients were not on any anti-epileptic drugs. 72% of the cases had duration of epilepsy for less than 10 years in a study done by GoelP et al., 2006²⁷.

Out of 130 studied women, 41 (31.5%) were using Lamotrigine as antiepileptic drug in pregnancy, 14 (10.8%) were using Carbamazepine, 11 (8.5%) each were using Levitracetam and Levitracetam + clobazam combination, 9 (6.9%) women were using Carbamazepine+clobazam. 8 (6.2%) women used sodium valproate, 6 (4.6%) used phenytoin+clobazam, 5 (3.8%) used phenytoin sodium, 3 (2.4%) were having Sodium valproate+clobazam, 2 (1.5%) women used Sodium valproate+Levodopa. 20 (15.4%) women were not on epileptic treatment. In a study done by Nibedita C et al (2008)²⁸ the anticonvulsants used 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 6 (already). Similar results were also observed by Raji C et al (2017)²⁶ in their study. Majority of women in their study were using Carbamazepine (31.82%), followed by Carbamazepine + clobazam (22.73%). 13.64% women were not using any antiepileptic treatment.

Maternal complications included gestational hypertension in 28 (21.5%), PROM in 10 (7.7%), GDM in 5 (3.8%), Abruptio placenta and hypothyroid in 4 (3.1%) women each. In a study done by Raji C et al (2017)²⁶ most common maternal complication included was gestational diabetes in 20% women followed by PROM in 7.27% patients. GoelPet al. (2006)²⁷ in their study reported PIH in 24.3%, abruptio in 5.4%, GDM in 2.7% and induction of labour in 18.9% of cases in their study. Malik R et al. (2017)²⁹ conducted a study in which 38 cases had pregnancy related complications of which the most common was gestational hypertension in 22 (20%) cases. Out of 130 studied women, 74 (56.9%) had lower segment caesarean section followed by 46 (35.4%) normal vaginal delivery, 6 (4.6%) had vaginal assisted delivery and 4 (3.1%) had abortion. Our study is comparable with the findings of Nibeta C et al (2008)²⁸. In their study the rate of Cesarean section was higher i.e. 65.1% in these patients as they were high risk pregnancies with less fetal movements and also as some of the patients opted for the same. In a study done by Raji C et al (2017)²⁶, the rate of cesarean section was 28.18%, Labour natural in 62.72%. In present study, IUGR observed in 9.52% and preterm labour in 11.43% which is comparable to Nibedita C et al (2008)²⁸ observed IUGR (9.3%) and preterm labour in (9.3%) of cases.²⁹ In our study, there were 120 (92.3%) live births and 10 (7.7%) still births in our study. Birth weight was 2.5-3kgs in majority of neonates i.e. 82 (63.1%) followed by >3kg in 23 (17.7%) neonates. 14 (10.8%) neonates had 2-2.4kg weight whereas 11 (8.5%) neonates weighed <2kg. Raji C et al (2017)²⁶ in their study also observed live birth in 96 (91.43%) cases. Intrauterine Fetal death (IUID) occurred in 9 (8.57%) cases. 22 babies had birth weight <2.5 kg. Most of the babies had birth weight >2.5 kg. There were 25 (19.2%) low birth weight neonates followed by 13 (10.0%) premature. IUGR was seen in 12 (9.2%) neonates, still birth in 10 (7.7%) neonates, 3 (2.3%) neonates had birth asphyxia, 3 (2.3%) expired. Only 2 (1.5%) neonates had congenital anomaly. Prematurity occurred in 12 (11.43) babies. IUGR in 10 babies, Birth asphyxia in 2, Neonatal death in 2 in a study done by Raji C et al (2017)²⁶. Nibedita C et al (2009)²⁸ in their study also observed low birth in 23.3% neonates, prematurity in 18.6, IUGR in 9.3% and birth asphyxia in 2.3% neonates.

In our study of 130 patients only 2 (1.5%) was the maternal mortality. Out of the expired 2 mothers, one died due to meningioma brain and the other due to cardiac arrest (case of epilepsy with severe anemia leading to cardiac failure). In a study done by Raji C et al (2017)²⁶ one mother died due to Acute pulmonary edema due to severe preeclampsia. The frequency of death at delivery hospitalization was 80 deaths per 100 000 (0.080%) pregnancies for women with epilepsy in a study done by MacDonald SC et al (2015)³⁰ in their study pregnant women with epilepsy were 69,385.

Conclusion:-

Pregnancy with epilepsy presents a unique challenge both for the mother and the baby. The 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 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.

We can reassure women with epilepsy of a good fetomaternal outcome, comparable to that of the general population, except with respect to congenital malformations. The team approach by a neurologist and an obstetrician with special interests in this field is paramount to the care of women with epilepsy and should continue throughout the reproductive years for family planning, conception, the three trimesters of pregnancy, labor, delivery, and the postpartum period.

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