Sikha Pandey et al /J. Pharm. Sci. & Res. Vol.4(4), 2012, 1803-1806

ISSN:0975-1459
Journal of Pharmaceutical Sciences and Research
www.jpsr.pharmainfo.in

Foetal Outcome in Epileptic Women with Seizures during Pregnancy.

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Abstract
Objective - To assess whether seizures in women with epilepsy during pregnancy contribute to adverse pregnancy outcomes.
Methodology - A retrospective cross-sectional study. This study was conducted in Bundelkhand Medical College Sagar (M P) over a period of two years from 2008 to 2010.A total of 380 women with epilepsy were selected who had single births from 2008 to 2003 and who had been diagnosed with epilepsy within 2 years prior to their index delivery, together with 2410 matched women without chronic disease as a comparison cohort. Women with epilepsy were further stratified into 2 groups for analysis: women who did and did not have seizures during pregnancy.
Results — Compared with women without epilepsy, epileptic seizures during pregnancy were independently associated with a 1.36-fold (95% confidence interval [CI], 1.01-1.88), 1.63-fold (95% CI, 1.21-2.19), and 1.37-fold (95% CI, 1.09-1.70) increased risk of low-birth-weight infants, preterm delivery, and SGA, respectively, after adjusting for family income and parental and infant characteristics. Further, the risk of SGA increased significantly (odds ratio, 1.34; 95% CI, 1.01-1.84) for women with seizures during pregnancy compared with women with epilepsy who did not have seizures during pregnancy.
Main Outcome Measures Low-birth-weight infants, preterm delivery, and infants who are small for gestational age (SGA).
Conclusion - We suggest preventing seizures during pregnancy as an essential step to reduce risk of adverse pregnancy outcomes.
Key words – Epilepsy, Seizure, Pregnancy

INTRODUCTION

Epilepsy is the most common major neurologic complication in pregnancy, with estimated prevalence among pregnant women ranging from 0.2% to 0.7%.[1-3] While approximately 40% of the 18 million women with epilepsy (WWE) in the world are of child-bearing age, managing maternal epilepsy and monitoring the health of the developing fetus remain some of the most perplexing and engaging issues in the fields of neurology and obstetrics.[4]Although most WWE experience uncomplicated pregnancies,[5] increased incidence ofstillbirths, malformations, spontaneous abortions, and neonatal deaths have been reported for WWE compared with the general population.[6-9]

Previous literature reports that WWE are at higher risk of having low birth weight (LBW), preterm birth, and infants who are small for gestational age (SGA).[10-12.] Available data suggest that risks inherent in having seizures might be one factor contributing to the observed inappropriate fetal development or loss.[14-15] Thus, failing to distinguish the risk specifically attributable to epileptic seizures during pregnancy might explain these inconsistencies. Patterns and frequency of seizures during pregnancy vary among patients. About 60% of pregnant WWE remain seizure-free, while seizures increase in about one-fourth of them.[16-17]

This study aimed to assess the risk of epileptic seizures during pregnancy contributing to adverse pregnancy outcomes including LBW, preterm birth, and SGA infants compared with unaffected mothers. Both maternal and paternal characteristics were taken into consideration.

AIMS AND OBJECTIVES

1. To assess the risk of epileptic seizures during pregnancy contributing to adverse pregnancy out comes.
2. To Compare the risk of adverse pregnancy outcomes in women having seizures during pregnancy with the unaffected women.
3. To Study maternal Paternal Characteristics contributing to adverse pregnancy outcome.

MATERIALS AND METHODS

SELECTION OF SUBJECTS

Inclusion Criteria

Women Who had Single Births in Bundelkhand Medical College Sagar Between January 01 , 2008 and December 31st , 2010.

1. The Study Cohort of WWE was Identified by a Diagnosis of Either Epilepsy (International Classification of Diseases, Ninth Revision [ICD-9] code 345) or convulsions (ICD-9 code 780.3) from inpatient sources.
2. The Diagnosis of Epilepsy was conformed only if the women in the study cohort had three consecutive diagnosis of epilepsy or convulsion within two years prior to the index delivery

Exclusion Criteria

1. Women who did not history of three consecutive episodes of convulsion within two years prior to the index delivery.
2. Women with a diagnosis of another chronic diseases (such as hypertension, diabetes, any type of mental disorder, systemic lupus erythematosus, rheumatoid arthritis and gout).

Study Population

The participants were 28120 Women who had single births in BMC Between January 01 , 2008 and December 31st , 2010. The study cohort and comparison cohort were derived from this population.We Randomly Selected 2410 Women (8 for every women with epilepsy) Matched with the study cohort (women with epilepsy) In terms of age (<20 , 20-24, 25-29, 30-34, > 35 years) and years of delivery.

Methodology

We Stratified WWE in to 2 Categories :- Those who had seizures during pregnancy and those who did not. We Followed the pregnancy outcomes of the study and cohort group. Multiple outcome measures were evaluated with the result of each measure considered separately. Other Potential Confounders were also adjusted for in this study.

Evaluations And Follow Up

The study Population was compared in terms of maternal , Paternal and infant characteristics. Adverse pregnancy outcomes were noted and comparisons made amongst the study and the cohort group in our study.

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1. Adverse pregnancy outcomes included LBW (<2500 g), preterm birth (gestation <37 weeks), and SGA (birth weight below the 10th percentile for gestational age).
2. characteristics of the infant (sex and parity [1, 2, ≥3]).
3. Maternal Characteristics includes age and Higher Educational Level.
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Statistical Analysis

The SAS statistical package was used to perform the analyses in this study. We tested for differences in the characteristics of infants, mothers, and fathers among 3 cohorts using χ^2 tests. Multivariate logistic regression analyses were also performed to examine the risk of adverse pregnancy outcomes for the cohorts after adjusting for possible confounding factors. Finally, medication use might affect the results. Any WWE who received antiepileptic drugs (AEDs) during pregnancy were later included to approach a distribution closer to the real situation. The odds ratios (ORs) and 95% confidence intervals (CIs) for the estimated ORs were calculated. A 2-sided P <.05 was considered statistically significant.

RESULTS

In our Study Consistently Showed That Pregnant Women Who Experienced Seizures During Pregnancy had high Chance of Adverse Pregnancy outcomes Demographic data on the births are given in Table 1. Pearson χ^2 tests show that there were significant differences among epileptic women who had seizures during pregnancy, epileptic women without seizures during pregnancy, and the comparison cohort in terms of highest maternal educational level (P = .02), marital status (P = .04), and paternal age (P = .02). In addition, of the total 380 pregnant WWE, 184 (48.5%) experienced seizures during pregnancy. Table 2 describes the distribution and crude ORs of LBW, preterm, and SGA infants born to WWE who had seizures during pregnancy, those who did not, and the women in the comparison cohort. It consistently shows that WWE who had seizures during pregnancy had the highest percentage of LBW, preterm, and SGA infants of the 3 groups. Logistic regression analyses show that WWE who had seizures during pregnancy were more likely to have LBW (crude OR, 1.45; 95% CI, 1.06-2.00), preterm (crude OR, 1.68; 95% CI, 1.24-2.26), and SGA infants (crude OR, 1.44; 95% CI, 1.16-1.79) than women without epilepsy.

Table 1-Comprasion of Pregnant Women Without History of Chronic Disease and Pregnant Women With Epiliesy in Relation to Maternal , Paternal and infant Characteristics.

Variable	Pregnant Women. No. (%) (n=2790)		
		Epilepsy	
	No History of Chronic Disease (n=2410)	No Seizures During Pregnancy (n=196)	Seizures During Pregnancy (n=184)
Infant Characteristics			
Sex			
Male	1270(52.7)	105 (53.6)	90 (49.9)
Female	1140 (47.5)	91 (46.4)	94 (50.1)
Parity			
1	1316 (54.6)	106 (54.4)	99 (54.1)
2	785 (32.6)	66 (33.7)	60 (32.8)
≥3	309 (12.8)	24 (12.8)	25 (13.1)
Maternal Characteristics			
Age, Y			
<20	122 (5.1)	06 (3.3)	13 (7.0)
20-24	609 (25.3)	44 (22.8)	51 (27.8)
25-29	91 (37.8)	77 (39.2)	67 (36.4)
30-34	588 (24.4)	51 (26.3)	41 (22.5)
≥34	180 (7.4)	18 (8.4)	12 (6.4)
Paternal Characteristics			
Age, Y			
< 30	1043 (43.3)	81(41.3)	86(49.9)
30-34	843 (35.0)	67(34.5)	62 (34.0)
…34	524 (21.7)	48(24.2)	36 (19.1

Table 2 also illustrates the details of the adjusted ORs of LBW, preterm, and SGA infants for the 3 groups. After adjusting for the infant, maternal, and paternal characteristics, the ORs of LBW, preterm, and SGA infants for women with epileptic seizures during pregnancy were 1.36 (95% CI, 1.01-1.88), 1.63 (95%

CI, 1.21-2.19), and 1.37 (95% CI, 1.09-1.70) times compared with mothers in the comparison cohort. There was no significant difference in the risk of LBW and SGA infants between WWE who had no seizures during pregnancy and women without epilepsy, while the risks of preterm delivery increased to a mild extent (OR, 1.39; 95% CI, 1.03-1.93).

As for the effect size, compared with women in the comparison cohort, the birth weights of neonates of WWE with and without seizures during pregnancy decreased 76 g (95% CI, 35-117) and 24 g (95% CI, –17 to 65), respectively. In addition, the gestational weeks for WWE who did and did not have seizures during pregnancy were also reduced by 0.44 (95% CI, 0.24-0.64) and 0.13 (95% CI, –0.93 to 0.33) weeks, respectively (data not shown in table).

Table 2.Crud and Adjustment ORs for Preterm LBW, and SGA infants for Women With Epilepsy , Women With Epilepsy , and Women with Epileptic Seizures During Pregnancy.

Variable	Pregnant Women No (n=2790)	Pregnant Women With Epilepsy	
	No History of Chronic Disease (n=2410)	No Seizures During Pregnancy (n=196)	Seizures During Pregnancy (n=184)
LBW			
Yes	152 (6.3)	15 (7.6)	17 (9.0)
No	2258 (93.4)	181 (92.4)	167 (91.1)
Crude OR (95%Cl)	1 [Reference]	1.22 (0.87-1.71)	1.45 (1.06-2.00)[b]
Adjusted Or (95%Cl)[a]	1 [Reference]	1.19 (0.85-1.67)	1.36 (1.01-1.88)[b]
Preterm birth			
Yes	159 (6.6)	18 (9.2)	19 (10.5)
No	2251 (93.4)	178 (90.8)	165 (89.5)
Crude OR (95%Cl)	1 [Reference]	1.44 (1.05-1.96)[b]	1.68 (1.24-2.26)[c]
Adjusted Or (95%Cl)[a]	1 [Reference]	1.39 (1.03-1.93)[b]	1.63 (1.21-2.19)[c]
SGA			
Yes	400 (16.6)	33 (17.0)	41 (22.3)
No	2010 (83.4)	163 (83.0)	143 (77.7)
Crude OR (95%Cl)	1 [Reference]	1.03 (0.81-1.30)	1.44 (1.16-1.79)[c]
Adjusted Or (95%Cl)[a]	1 [Reference]	1.03 (0.80-1.32)	1.37 (1.09-1.70)[c]

Abbreviations CI. Confidence interval : LBW low birth weight OR odds ratio: SGA small for gestational age. Adjusted regression models include maternal characteristics (age. educational Level Marital Status). Infant characteristics (Sex. perity). parental age difference and level P<.05. P<0.001

Table .3-Crud and Adjustment ORs for Preterm LBW, and SGA infants for Women With Epilepsy Who Did and Did Not Have Epileptics Seizures During Pregnancy

Variable	Pregnant Women With Epilepsy , No (n=380)		
	No Seizures During Pregnancy (n=196)	No Seizures During Pregnancy (n=184)	P Value
LBW			
Yes	15(7.6)	16 (9.0)	
No	181 (92.4)	168 (91.0)	.44
Crude OR (95%Cl)	1 [Reference]	1.19 (0.76-1.87)	
Adjusted Or (95%Cl)[a]	1 [Reference]	1.16 (0.73-1.84)	
Preterm birth			
Yes	18(9.2)	19(10.5)	.46
No	178 (90.8)	165 (89.5)	
Crude OR (95%Cl)	1 [Reference]	1.17 (0.77-1.77)	
Adjusted Or (95%Cl)[a]	1 [Reference]	1.12 (0.73-1.77)	
SGA			
Yes	33 (17.0)	41 (22.3)	
No	163 (83.0)	143 (77.7)	
Crude OR (95%Cl)	1 [Reference]	1.40 (1.03-1.92)[b]	.03
Adjusted Or (95%Cl)[a]	1 [Reference]	1.34 (1.01-1.84)[b]	

Abbreviations CI. Confidence interval : LBW low birth weight OR odds ratio: SGA small for gestational age. [a] Adjusted regression models include maternal characteristics (age. educational Level Marital Status). Infant characteristics (Sex.perity). parental age difference and level [b]P<.05.

This study distinguishes the risk of adverse fetal outcomes for WWE who did and did not have seizures during pregnancy. Our study reveals that compared with pregnancy outcomes for women without chronic disease, seizures during pregnancy were independently associated with 1.63-, 1.36-, and 1.37-fold increased risk of neonates being delivered preterm, of LBW, and SGA, respectively.Analysing WWE in greater detail, the odds of SGA for women with epileptic seizures during pregnancy were 1.34 times those of WWE without seizures during pregnancy.

DISCUSSION

Similar patterns of risks remained, even when WWE who received AEDs during pregnancy were included in the analysis. Approximately half of the WWE in our study remained seizure free throughout pregnancy. Numerous physiological and psychological changes might influence the number of seizures during pregnancy. Sleep deprivation, rapid weight gain, new stresses, and biological factors such as metabolic, hormonal, or hematologic changes occurring in pregnancy might play significant roles in seizures.[19] During pregnancy, sex hormone concentrations reach a very high level. With estrogen having epileptogenic effects and progesterone having both convulsant and anticonvulsant properties, sex hormones may factor into the frequency of maternal seizures.[20] The effects of sociodemographic characteristics could also be a concern.

For example, maternal age was associated with adverse pregnancy outcomes for women with and without epilepsy.[21] In our study, WWE had significantly lower education levels than unaffected women. Several mechanisms might explain the link between seizures and pregnancy outcomes; trauma and placental hypoperfusion are 2 of the most frequently mentioned. Trauma caused by unexpected seizures might result in ruptured fetal membranes with elevated risks of infection, premature delivery, and even fetal death.[24] Abruption of placentae is reported to occur after 1% to 5% of minor and 20% to 50% of major blunt injuries.[25] Previous studies also identified seizures as producing fetal heart rate depression, fetal hypoxia with resultant acidosis, and fetal intracranial hemorrhage.[13, 26-27] Minkoff et al[26] described 1 intrauterine death attributed to fetal intracranial hemorrhage occurring after a seizure episode. Both partial and generalized convulsive status epilepticus have been linked with fetal hypoxia, bradycardia, and antenatal death.[28-29], reducing risk among WWE might begin with preconception planning, specifically, maintaining seizure control for a period of time before pregnancy.

Second, sleep deprivation, whether due to nocturia, physical discomfort, or personal doubt, might provoke seizures during pregnancy.[31] Third, noncompliance with antiepileptic medication therapy played a clear role in the increased frequency of seizures during pregnancy.[5] Appropriate education about the risks of seizures vs AEDs might help WWE adopt effective strategies for controlling their epilepsy during pregnancy. Finally, other factors such as improved strategies for coping with stress might also aid seizure control.

CONCLUSION

Our study leads the way in examining and differentiating pregnancy outcomes among WWE who do and do not have seizures during pregnancy. Our study confirmed that seizure control during pregnancy should remain the primary goal of management. The obstetrician and physician should work together prior to conception and throughout the pregnancy to closely monitor seizures and contributing factors (eg, sleepdeprivation and medication.

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