

Affect of Seizures During Gestation on Pregnancy Outcomes in Women With Epilepsy

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Objective: To assess whether seizures in women with epilepsy during pregnancy contribute to adverse pregnancy outcomes.

Design: A retrospective cross-sectional study.

Setting: Taiwan.

Patients: This study linked 2 nationwide population-based data sets: Taiwan's birth certificate registry and the Taiwan National Health Insurance Research Data set. A total of 1016 women with epilepsy were selected who had single births from 2001 to 2003 and who had been diagnosed with epilepsy within 2 years prior to their index delivery, together with 8128 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.

Main Outcome Measures: Low-birth-weight in-

fants, preterm delivery, and infants who are small for gestational age (SGA).

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.

Conclusion: We suggest preventing seizures during pregnancy as an essential step to reduce risk of adverse pregnancy outcomes.

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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 of stillbirths, malformations, spontaneous abortions, and neonatal deaths have been reported for WWE compared with the general population.⁶⁻⁹ Contradictory data have been published for other prevalent adverse fetal outcomes. 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 Nevertheless, studies by Viinikainen et al³ and Hiilesmaa et al¹³

found no significant differences between WWE and controls in terms of the risks of preterm delivery and reduced birth weights, but did find a higher rate of SGA infants. 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.

No study to date has specifically distinguished the extent to which maternal epileptic seizures during pregnancy pose a risk to the fetus. 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} More research in this area is imperative because improvements in optimal management strategies for pregnant WWE could produce significant health benefits for both mothers and infants.

This study aimed to assess the risk of epileptic seizures during pregnancy con-

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tributing to adverse pregnancy outcomes including LBW, preterm birth, and SGA infants compared with unaffected mothers. Both maternal and paternal characteristics were taken into consideration.

METHODS

DATABASE

This study used Taiwan's National Health Insurance Research Data set (NHIRD), which was linked to the Taiwan birth certificate registry. The NHIRD, published by the National Health Research Institute, consists of monthly summaries of inpatient and ambulatory care claims for more than 22 million enrollees, representing more than 98% of the island's population. In addition, the NHIRD includes a registry of contracted beds, medical facilities, board-certified specialists, and beneficiaries. The NHIRD is one of the largest databases currently available anywhere and presents a unique opportunity to systematically explore the association between adverse pregnancy outcomes and maternal epileptic seizures.

Information from the birth certificate registry included birth dates for both infants and their parents, gestational week at birth, infant birth weight, sex, parity, place of birth, parental educational levels, and maternal marital status. Because the registration of all births is mandatory in Taiwan, the data in the birth certificate registry are believed to be extremely accurate and comprehensive.

With assistance from the Bureau of National Health Insurance (NHI) in Taiwan, the mothers' and infants' unique personal identification numbers provided links between the NHIRD and birth certificate data. Confidentiality was addressed by abiding by the data regulations of the bureau. All personal identifiers were encrypted by the bureau before release to the researchers. Because the NHIRD consists of secondary data rendered unidentifiable that was released to the public for research purposes, this study was exempt from full review by the internal review board.

STUDY SAMPLE

The participants were 477 006 women who had single births in Taiwan between January 1, 2001, and December 31, 2003. 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 or ambulatory care claims between 1998 and 2003 (n=2504). To ensure the validity of epilepsy diagnoses, women in the study cohort had at least 3 consensus diagnoses of epilepsy or convulsions within 2 years prior to the index delivery. We also excluded women with a diagnosis of another chronic disease (such as hypertension, diabetes, any type of mental disorder, systemic lupus erythematosus, rheumatoid arthritis, gout, sarcoidosis, or ankylosing spondylitis) (n=10) that could increase the risk of adverse pregnancy outcomes. In addition, we excluded women who received antiepileptic drugs (n=166), leaving 1016 WWE for analysis.

The comparison cohort was derived from the remaining women. Again, we excluded women who had been diagnosed with any type of chronic disease between 1998 and 2003. We then randomly selected 8128 women (8 for every woman with epilepsy) matched with the study cohort (women with epilepsy) in terms of age (<20, 20-24, 25-29, 30-34, and ≥35 years) and year of delivery.

VARIABLES OF INTEREST

For this study, we stratified WWE into 2 categories: those who had seizures during pregnancy and those who did not. We de-

defined women with seizures during pregnancy as those who were hospitalized or treated in the emergency department for epilepsy during pregnancy. Adverse pregnancy outcomes included LBW (<2500 g), preterm birth (gestation <37 weeks), and SGA (birth weight below the 10th percentile for gestational age). Savitz et al¹⁸ proposed a lack of concordance among these adverse pregnancy outcomes. Multiple outcome measures should be evaluated, with the results from each measure considered separately. Our study thus adopted multiple outcomes for assessment.

Other potential confounders were also adjusted for in this study. These included characteristics of the infant (sex and parity [1, 2, ≥3]), mother (age, highest educational level [elementary school or lower, junior high school, senior high school, college or above], and marital status [married and other]), father (age and highest educational level [elementary school or lower, junior high school, senior high school, college or above] and family monthly income [in US dollars] <\$445.00, \$445.00-\$890.00, \$890.01-\$1480.00, ≥\$1480.01; based on an exchange rate from the year 2001 of \$1 US=\$33.8 New Taiwan).

STATISTICAL ANALYSIS

The SAS statistical package (SAS System for Windows, version 8.2; SAS Institute Inc, Cary, North Carolina) 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 (ie, 104 WWE without seizures and 62 WWE with seizures) 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

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 ($P = .04$), family monthly income ($P < .001$), and paternal age ($P = .02$). In addition, of the total 1016 pregnant WWE, 503 (49.5%) 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 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 char-

acteristics, 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).

We estimated the proportions and risks of adverse pregnancy outcomes, comparing WWE with and without seizures during pregnancy (**Table 3**). The proportion of SGA infants was significantly higher for WWE who had seizures during pregnancy compared with epileptic women who did not. After adjusting for listed covariates, the risk of SGA increased significantly (OR, 1.34; 95% CI, 1.01-1.84) for women with seizures during pregnancy compared with WWE who remained seizure-free during pregnancy.

Furthermore, even after adding WWE who received AED treatment during pregnancy (ie, 104 WWE without seizures and 62 WWE with seizures), we still found that WWE who had seizures during pregnancy had higher odds of preterm birth and LBW and SGA infants than women without epilepsy in the comparison cohort (**Table 4**).

COMMENT

This is the first study to distinguish the risk of adverse fetal outcomes for WWE who did and did not have seizures during pregnancy. Our nationwide population-based 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. Analyzing 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. Similar patterns of risks remained, even when WWE who received AEDs during pregnancy were included in the analysis.

Neonates born preterm, of LBW, and SGA may be predisposed to diseases during infancy and later life, highlighting the significance of proper intervention strategies for prevention. Although some prior studies reported increased incidence of adverse fetal outcomes such as preterm delivery, LBW, and SGA among WWE, others demonstrated no statistically significant difference between women with and without epilepsy.^{3,10-13} Our study further illuminates these conflicting data to suggest that it is the seizures themselves that seem to contribute greatly to the increased risk of infants being delivered preterm, of LBW, and SGA. For women who remained seizure-

Table 1. Comparison of Pregnant Women Without History of Chronic Disease and Pregnant Women With Epilepsy in Relation to Maternal, Paternal, and Infant Characteristics in Taiwan, 2001-2003

Variable	Pregnant Women, No. (%) (n=9144)		
	No History of Chronic Disease (n=8128)	Epilepsy	
		No Seizures During Pregnancy (n=513)	Seizures During Pregnancy (n=503)
Infant characteristics			
Sex			
Male	4269 (52.7)	275 (53.6)	251 (49.9)
Female	3859 (47.5)	238 (46.4)	252 (50.1)
Parity			
1	4435 (54.6)	279 (54.4)	272 (54.1)
2	2654 (32.6)	173 (33.7)	165 (32.8)
≥3	1039 (12.8)	61 (11.9)	66 (13.1)
Maternal characteristics			
Age, y			
<20	416 (5.1)	17 (3.3)	35 (7.0)
20-24	2056 (25.3)	117 (22.8)	140 (27.8)
25-29	3072 (37.8)	201 (39.2)	183 (36.4)
30-34	1984 (24.4)	135 (26.3)	113 (22.5)
≥34	600 (7.4)	43 (8.4)	32 (6.4)
Educational level			
≤Elementary school	157 (1.9)	14 (2.7)	12 (2.4)
Junior high school	1299 (16.0)	96 (18.7)	103 (20.5)
Senior high school	5638 (69.4)	345 (67.3)	340 (67.6)
≥College	1034 (12.7)	58 (11.3)	48 (9.5)
Marital status			
Married	7873 (96.9)	497 (96.9)	477 (94.8)
Other	255 (3.1)	16 (3.1)	26 (5.2)
Family income, US \$/mo			
<445.00	3311 (40.7)	179 (34.9)	230 (45.7)
445.00-890.00	1986 (24.4)	146 (28.5)	134 (26.6)
890.01-1480.00	1838 (22.6)	145 (28.3)	105 (20.9)
≥1480.01	993 (12.2)	43 (8.4)	34 (6.8)
Paternal characteristics			
Age, y			
≤30	3517 (43.3)	212 (41.3)	236 (46.9)
30-34	2841 (35.0)	177 (34.5)	171 (34.0)
≥34	1770 (21.7)	124 (24.2)	96 (19.1)
Educational level			
≤Elementary school	123 (1.5)	10 (2.0)	13 (2.6)
Junior high school	1599 (19.7)	120 (23.4)	110 (21.9)
Senior high school	5057 (62.2)	316 (61.6)	313 (62.2)
≥College	1349 (16.6)	67 (13.0)	67 (13.3)

free throughout pregnancy, null or mild risk was identified compared with unaffected women. However, it is worth noting that although increased risks were observed in women with active seizures during pregnancy, most WWE have normal pregnancy outcomes.

Approximately half of the WWE in our study remained seizure free throughout pregnancy. Similarly, in a pregnancy registry in Norway, most mothers with epilepsy remained seizure free (63%), while another 17% experienced increased seizure frequencies.¹⁷ 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 sei-

Table 2. Crude and Adjusted ORs for Preterm, LBW, and SGA Infants for Women Without Epilepsy, Women With Epilepsy, and Women With Epileptic Seizures During Pregnancy, 2001-2003

Variable	Pregnant Women, No. (%) (n=9144)		
	No History of Chronic Disease (n=8128)	Epilepsy	
		No Seizures During Pregnancy (n=513)	Seizures During Pregnancy (n=503)
LBW			
Yes	515 (6.3)	39 (7.6)	45 (9.0)
No	7613 (93.4)	474 (92.4)	458 (91.1)
Crude OR (95% CI)	1 [Reference]	1.22 (0.87-1.71)	1.45 (1.06-2.00) ^b
Adjusted OR (95% CI) ^a	1 [Reference]	1.19 (0.85-1.67)	1.36 (1.01-1.88) ^b
Preterm birth			
Yes	534 (6.6)	47 (9.2)	53 (10.5)
No	7594 (93.4)	466 (90.8)	450 (89.5)
Crude OR (95% CI)	1 [Reference]	1.44 (1.05-1.96) ^b	1.68 (1.24-2.26) ^c
Adjusted OR (95% CI) ^a	1 [Reference]	1.39 (1.03-1.93) ^b	1.63 (1.21-2.19) ^c
SGA			
Yes	1349 (16.6)	87 (17.0)	112 (22.3)
No	6779 (83.4)	426 (83.0)	391 (77.7)
Crude OR (95% CI)	1 [Reference]	1.03 (0.81-1.30)	1.44 (1.16-1.79) ^c
Adjusted OR (95% CI) ^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.

^aAdjusted regression models include maternal characteristics (age, educational level, marital status), infant characteristics (sex, parity), family monthly income, parental age difference, and paternal educational level.

^b $P < .05$.

^c $P < .001$.

Table 3. Crude and Adjusted ORs for Preterm, LBW, and SGA Infants for Women With Epilepsy Who Did and Did Not Have Epileptic Seizures During Pregnancy, 2001-2003

Variable	Pregnant Women With Epilepsy, No. (%) (n=1016)		P Value
	No Seizures During Pregnancy (n=513)	Seizures During Pregnancy (n=503)	
	LBW		
Yes	39 (7.6)	45 (9.0)	
No	474 (92.4)	458 (91.0)	
Crude OR (95% CI)	1 [Reference]	1.19 (0.76-1.87)	
Adjusted OR (95% CI) ^a	1 [Reference]	1.16 (0.73-1.84)	
Preterm birth			.46
Yes	47 (9.2)	53 (10.5)	
No	466 (90.8)	450 (89.5)	
Crude OR (95% CI)	1 [Reference]	1.17 (0.77-1.77)	
Adjusted OR (95% CI) ^a	1 [Reference]	1.12 (0.73-1.71)	
SGA			.03
Yes	87 (17.0)	112 (22.3)	
No	426 (83.0)	391 (77.7)	
Crude OR (95% CI)	1 [Reference]	1.40 (1.03-1.92) ^b	
Adjusted OR (95% CI) ^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.

^aAdjusted regression models include maternal characteristics (age, educational level, marital status), infant characteristics (sex, parity), family monthly income, parental age difference, and paternal educational level.

^b $P < .05$.

zures.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, WVE had significantly lower education levels than unaffected women. Previous studies have indeed identified an association between epilepsy and poor academic performance and educational underachievement.^{22,23} Thus, to obtain more appropriate estimates, the multivariate regression analyses adjusted for sociodemographic traits such as family income and maternal age and educational and marital status.

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 Abruptio of placenta 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 al²⁶ 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} Although it is believed that tension and acute injury may result from strong uterine contractions and vascular compromise caused by maternal seizures, contributing to fetal distress and hindering development, more research should specifically examine how seizures during pregnancy increase the risk of neonates being of LBW and SGA.

Table 4. Adjusted ORs for Preterm, LBW, and SGA Infants for Pregnant Women Without Epilepsy, Women With Epilepsy, and Women With Epileptic Seizures During Pregnancy, 2001-2003

Variable	Pregnant Women, No. (%) (n=9310)		
	No History of Chronic Disease (n=8128)	Epilepsy ^a	
		No Seizures During Pregnancy (n=617)	Seizures During Pregnancy (n=565)
LBW			
Yes	515 (6.3)	46 (7.5)	50 (8.9)
No	7613 (93.4)	571 (92.5)	515 (91.1)
Crude OR (95% CI)	1 [Reference]	1.19 (0.87-1.63)	1.44 (1.06-1.95) ^c
Adjusted OR (95% CI) ^b	1 [Reference]	1.15 (0.84-1.58)	1.36 (1.01-1.85) ^c
Preterm birth			
Yes	534 (6.6)	54 (8.8)	60 (10.6)
No	7594 (93.4)	563 (91.2)	505 (89.4)
Crude OR (95% CI)	1 [Reference]	1.36 (1.02-1.83) ^c	1.69 (1.28-2.24) ^d
Adjusted OR (95% CI) ^b	1 [Reference]	1.33 (0.99-1.79)	1.65 (1.24-2.19) ^d
SGA			
Yes	1349 (16.6)	108 (17.5)	127 (22.5)
No	6779 (83.4)	509 (82.5)	438 (77.5)
Crude OR (95% CI)	1 [Reference]	1.07 (0.85-1.32)	1.46 (1.19-1.79) ^d
Adjusted OR (95% CI) ^b	1 [Reference]	1.06 (0.86-1.32)	1.39 (1.13-1.71) ^d
SGA excluding LBW			
Yes	834 (10.3)	62 (10.1)	77 (13.6)
No	7294 (89.7)	555 (89.9)	488 (86.4)
Crude OR (95% CI)	1 [Reference]	0.98 (0.74-1.28)	1.38 (1.07-1.77) ^c
Adjusted OR (95% CI) ^b	1 [Reference]	0.99 (0.76-1.31)	1.33 (1.03-1.71) ^c

Abbreviations: CI, confidence interval; LBW, low birth weight; OR, odds ratio; SGA, small for gestational age.

^aIncluding those receiving treatment during pregnancy.

^bAdjusted regression models include maternal characteristics (age, educational level, marital status), infant characteristics (sex, parity), family monthly income, parental age difference, and paternal educational level.

^c $P < .05$.

^d $P < .001$.

There are significant implications of this study. Our results provided a compelling reason for preventing epilepsy attacks during pregnancy as an essential step of clinical practice to reduce risks of adverse pregnancy outcomes among WWE. Although frequency of maternal epileptic seizures during gestation cannot be predicted well based on factors such as age, ethnic origin, number of pregnancies, seizure type, use of AEDs, and seizure frequency during a previous pregnancy,⁵ certain modifiable factors may be considered for seizure control. First, several prospective studies have reassuring findings, suggesting that with effective seizure control, WWE can dramatically lower their risk of adverse pregnancy outcomes.^{16,30} Thus, 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 Inquiring about and resolving sleep difficulties as part of clinical practice might therefore facilitate maternal seizure control. Third, noncompliance with antiepileptic medication therapy played a clear role in the increased frequency of seizures during pregnancy.⁵ As all of the commonly used AEDs are teratogenic to some degree,^{1,32} fetal risk from uncontrolled seizure has to be balanced against the potential adverse effects of AED. Our study revealed that significantly more WWE who remained seizure-free during pregnancy took AEDs (16.9%), compared with the percentage of those who experienced seizures who were

taking AEDs (11% receiving AED treatment; $P = .004$). We stress the importance of maintaining an absence of seizures throughout pregnancy as a goal of clinical practice. 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 and quitting smoking might also aid seizure control. For example, Hvas et al³³ demonstrated that WWE who smoked were at even higher risk of preterm delivery and low birth weight than smokers without epilepsy.

Our study leads the way in examining and differentiating pregnancy outcomes among WWE who do and do not have seizures during pregnancy. In addition, our study addressed increasing concern about the effects of paternal characteristics (eg, paternal age or parental age difference) on adverse birth outcomes that may be independent of maternal effects.³⁴

Four limitations of this study merit attention. First, the NHIRD database only represented patients who had sought treatment for epilepsy. Although incomplete patient records should be a concern, epilepsy diagnoses were considered reliable because of the severe and specific reality of the disease interfering with childbearing. Though more than half of pregnancies might be unplanned,⁵ our study likely recruited a group of WWE who had milder disease and planned childbearing. Second, traits of WWE who did have seizures during pregnancy might not be the same as those who did not. Pregnant WWE who had seizures were

defined as those who were hospitalized or treated in the emergency department for epilepsy during pregnancy. While WWE who had seizures during pregnancy must have had fairly severe ones to prompt medical care, those who did not visit an emergency department for seizures during gestation were likely to also have had occasional and mild seizures. The risk of adverse pregnancy outcomes comparing these 2 groups of WWE might thus be underestimated. Third, in our attempt to examine risk of epilepsy for fetal outcomes taking AED use into consideration, it is possible that the group of WWE taking no AEDs are not the same as the group of women who required AEDs during pregnancy. Those WWE who were prescribed AEDs might also stop medication without consulting with their physicians. In addition, information on over-the-counter drug use among WWE was unavailable for our study. However, because the National Health Insurance program in Taiwan covers the cost of medication, it is expected that most AED use among WWE was prescribed and reported in the claims data set. Finally, some important variables that are likely to be associated with seizures and adverse pregnancy outcomes were not available in the NHIRD, such as cigarette smoking, maternal body mass index, age when seizures started, dietary behaviors, and sleep deprivation during pregnancy.

Our study confirmed that seizure control during pregnancy should remain the primary goal of management. As seizures occur in approximately 40% to 50% of all pregnant WWE, intervention should be carried out to protect the fetus as much as possible. The obstetrician and neurologist should work together prior to conception and throughout the pregnancy to closely monitor seizures and contributing factors (eg, sleep deprivation and medication compliance). Future studies are needed to replicate the results and elucidate the mechanisms, still indistinct, connecting seizures during pregnancy to adverse fetal outcomes such as LBW and SGA. Future studies may address concerns about whether seizures or medications lead to risk of miscarriage and fetal malformation.

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