



# The clinical characteristics of pregnant women with epilepsy in China

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**Background:** Epilepsy during pregnancy and puerperium is infrequent, and it can induce severe complications and poor prognosis. Pregnancy in women with epilepsy (WWE) is usually uneventful. Previous studies have mainly focused on the effects of different treatments on prognosis. However, few articles have addressed if different epilepsy types were associated with a higher incidence of seizure breakthrough/recurrence and pregnancy outcomes.

**Methods:** In the present study, based on a unique sample with a low incidence of epilepsy, we evaluated the main clinical characteristics of epilepsy patients.

**Results:** Mean age of pregnant WWE was  $29.95 \pm 4.65$  (range, 21–42) years. Pregnancies were at a mean gestational age of  $33.80 \pm 9.14$  (range, 7–41) weeks, and 85.24% (52/61) of WWE were in their third trimester. There was 9.84% (6/61) of pregnant WWE underwent abortion or induced labor in mid-pregnancy to ensure maternal safety. There was 75.41% (46/61) of pregnant WWE using antiepileptic drugs (AEDs), of which 52.46% (32/61) were taking a single AED and 22.95% (14/61) were using multiple AEDs. There was 47.54% (29/61) of WWE experiencing seizures during their pregnancy. We found that the type of epilepsy did not affect seizures during pregnancy or the prognosis. However, more pregnant WWE with hypertensive disorder had seizures compared with pregnant WWE without hypertensive disorder.

**Conclusions:** The study highlighted a novel direction for effectively improving seizures during pregnancy and the prognosis of pregnancy-associated epilepsy.

**Keywords:** Pregnancy; epilepsy; pregnancy outcome

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## Introduction

Approximately 6.1% of pregnant women have a history of epilepsy (1). Pregnancy in women with epilepsy (WWE) is usually uneventful (2), however, complications that impact maternal and fetal health can occur (3). Most studies in pregnant WWE have focused on antiepileptic drug (AED) therapy due to the risk of teratogenic effects

on the developing fetus. Few studies have described the demographic and clinical characteristics of pregnant WWE and investigated the influence of the type of epilepsy and hypertensive disorder of pregnancy (HDP) on complications in pregnant WWE.

The objective of this study was to describe the demographic and clinical characteristics of pregnant WWE and evaluate maternal and fetal outcomes, which will provide

**Table 1** Clinical characteristics and pregnancy outcomes of pregnant WWE (n=61)

Variables	Value
Age (years)	29.95±4.65
Gestational age (weeks)	33.80±9.14
Gravidity	1.77±1.00
Parity	1.20±0.65
AED use, % [n]	
Monotherapy	52.46 [32]
Polytherapy	22.95 [14]
Did not use AEDs	24.59 [15]
Incidence of seizures	47.54 [29]
Type of epilepsy, % [n]	
Genetic	67.21 [41]
Non-genetic	32.79 [20]
Gestational age, % [n]	
Early pregnancy	8.20 [5]
Second trimester	6.56 [4]
Third trimester	85.24 [52]
Maternal complications, % [n]	
HDP	14.75 [9]
Mortality	1.64 [1]
Perinatal outcomes	
Malformation, % [n]	1.64 [1]
Abortion and induced labor, % [n]	9.84 [6]
Prematurity, % [n]	13.11 [8]
Term delivery, % [n]	75.41 [46]
Intrauterine death, % [n]	1.64 [1]
Mortality, % [n]	1.64 [1]
Mean newborn weight (g)	3,123.37±610.2
Average Apgar score of the newborns	9.71±0.77
Mode of delivery, % [n]	
Cesarean section	80.33 [49]
Vaginal delivery	19.67 [12]

WWE, women with epilepsy; HDP, hypertensive disorder of pregnancy.

pre-pregnancy counseling and management in WWE, as well as prenatal and postpartum care of pregnant WWE.

We present the following article in accordance with the STROBE reporting checklist (available at <http://dx.doi.org/10.21037/apm-19-341>).

## Methods

The study conformed to the provisions of the Declaration of Helsinki (as revised in 2013). This study was approved by Institutional Research Ethics Committee of Beijing Tiantan Hospital (No. KY 2019-029-02). Requirements for written informed consent were waived because all personal data were de-identified before the analyses.

Medical records of pregnant women with a history of epilepsy who attended the Beijing Tiantan Hospital, China, from January 2004 to December 2017 were retrospectively reviewed. Inclusion criteria were: (I) in-hospital delivery at Beijing Tiantan Hospital; and (II) a diagnosis of epilepsy according to the 2014 International League Against Epilepsy (ILAE) criteria (4).

Maternal and fetal demographic and clinical characteristics and pregnancy outcomes were recorded. In subgroup analyses, the impact of the etiology of epilepsy on maternal and fetal outcomes was explored by stratifying the study sample according to genetic *vs.* non-genetic basis of epilepsy. A genetic basis of epilepsy was assumed from family history or characteristic signs and symptoms. The impact of HDP (pre-eclampsia, eclampsia, gestational hypertension, and chronic hypertension) on maternal and fetal outcomes was explored by stratifying the study sample based on the presence or absence of HDP, diagnosed according to American College of Obstetricians and Gynecologists criteria (5).

Statistical analyses were performed using SPSS version 20. Between group differences for data with a normal distribution were evaluated with unpaired *t*-tests. Comparisons of categorical data were performed with the chi-squared test.  $P < 0.05$  was considered as statistically significant.

## Results

### *Demographic and clinical characteristics WWE*

The medical records of 61 pregnant WWE were retrospectively reviewed. During study period, 0.25% (61/23,721) of pregnant women attending the Beijing Tiantan Hospital had a history of epilepsy. Baseline demographic and clinical characteristics of the study samples were shown in *Table 1*. Mean age of pregnant WWE was 29.95±4.65 (range, 21–42) years. Pregnancies were at a mean gestational age of 33.80±9.14 (range, 7–41) weeks, and 85.24% (52/61) of WWE were in their third trimester. There was 9.84% (6/61) of pregnant WWE underwent

**Table 2** Admission data and outcomes according to type of epilepsy

Variables	Genetic (n=41)	Non-genetic (n=20)	P
Age (years)	29.73±4.54	30.40±4.97	0.06
Gestational age (weeks)	34.93±8.44	31.60±10.33	0.22
Gravidity			0.47, Z=-0.72
Parity			0.88, Z=-0.16
Incidence of seizures, % [n]	51.22 [21]	40.00 [8]	0.41
Mode of delivery			
Cesarean section, % [n]	80.49 [33]	80.00 [16]	1.00
Perinatal outcome			
Malformation, % [n]	0	5.00 [1]	0.33
Abortion and induced labor, % [n]	4.88 [2]	20.00 [4]	0.08
Premature, % [n]	12.20 [5]	15.00 [3]	1.00
Term delivery, % [n]	80.49 [33]	65.00 [13]	0.22
Intrauterine death, % [n]	0	5.00 [1]	0.33
Mortality, % [n]	0	5.00 [1]	0.33
Mean weight (g)	3,238.61±513.35	2,841.56±729.95	0.06
Average Apgar score of the newborns			0.67, Z=-0.42

abortion or induced labor in mid-pregnancy to ensure maternal safety. There was 75.41% (46/61) of pregnant WWE using AEDs, of which 52.46% (32/61) were taking a single AED and 22.95% (14/61) were using multiple AEDs. There was 47.54% (29/61) of WWE experiencing seizures during their pregnancy.

Epilepsy was genetic in 67.21% (41/61) of pregnant WWE. There were no significant differences in maternal variables, including age, median gestational age, gravidity, parity, or the incidence of seizures in pregnant women with a genetic or non-genetic basis for their epilepsy. Similarly, there were no significant differences in mode of delivery or perinatal outcomes (*Table 2*).

There was 14.75% (9/61) of pregnant WWE experienced HDP. The incidence of seizures was significantly higher in pregnant WWE with HDP compared with those without ( $P=0.01$ ). There were no significant differences in maternal variables, including age, median gestational age, gravidity, or parity, or in mode of delivery or perinatal outcomes (*Table 3*).

## Discussion

This study described the demographic and clinical

characteristics of pregnant WWE. Mean age of pregnant WWE was less than 30 years. The majority of pregnant WWE used AED therapy during their pregnancy, and approximately 50% experienced seizures. Maternal and fetal outcomes were compared in pregnant WWE stratified by genetic or non-genetic basis of epilepsy and presence or absence of HDP. Type of epilepsy did not appear to affect maternal and fetal outcomes, but the incidence of seizures was significantly higher in pregnant WWE with HDP compared with those without.

Epilepsy is a chronic brain disorder characterized by the sudden onset of seizures caused by sudden abnormal neuronal firing. To our knowledge, the present study includes the largest sample of Chinese pregnant WWE reported to date. The study was conducted at Beijing Tiantan Hospital, a medical transport center for pregnant and postpartum patients with critical craniocerebral disease. The proportion of patients with epilepsy was expected to be higher than in other hospitals in Beijing. The incidence rate (0.25%) is lower than that reported for the UK, where an estimated 0.6% of pregnancies were in WWE, according to the 2011 report of the United Kingdom Confidential Enquiries into Maternal Deaths (6).

**Table 3** The impact of HDP on maternal and fetal outcomes

Variables	HDP group (n=9)	Other group (n=52)	P
Age (years)	29.67±3.71	30.08±4.85	0.81
Gestational age (weeks)	36.78±2.39	32.40±10.75	0.23
Gravidity			0.05, Z=-1.94
Parity			0.17, Z=-1.36
Incidence of seizures, % [n]	88.89 [8]	40.38 [21]	0.01
Mode of delivery, % [n]			
Cesarean section	88.89 [8]	78.85 [41]	0.67
Perinatal outcomes			
Abortion and induced labor, % [n]	0	11.54 [6]	0.58
Prematurity, % [n]	33.33 [3]	9.62 [5]	0.09
Term delivery, % [n]	66.67 [6]	76.92 [40]	0.68
Intrauterine death, % [n]	0	1.92 [1]	1.00
Mean weight (g)	2,960.00±789.46	3,157.56±571.51	0.38
Average Apgar score of the newborns			0.94, Z=-0.08

HDP, hypertensive disorder of pregnancy.

Pregnant WWE have an increased risk of adverse events compared with those without epilepsy, including preeclampsia, preterm labor, stillbirth, spontaneous abortion, vaginal bleeding, hypertension, postpartum hemorrhage, placental abruption, and an increased risk of cesarean delivery. Severe cases may even result in maternal death (7). In the present study, we reported one maternal death, for a case mortality rate of 1.64%. A previous retrospective cohort study conducted using the 2007–2011 Nationwide Inpatient Sample in the US found that pregnant WWE had a 10-fold increased risk of death compared with those without epilepsy (3).

The seizures that characterize epilepsy and the use of AEDs can result in poor maternal, fetal, and neonatal outcomes. Maternal seizures can not only cause maternal injury and obstetric sequelae like placental abruption, premature labor, and delivery, but also lead to hypoxia in the fetus and transient late decelerations, decreased beat-to-beat variability, and compensatory tachycardia (8). AEDs can have teratogenic and long-term neurodevelopmental effects on the fetus. Taken together, these data emphasize the importance of appropriate preconception consultation, counseling, and planning of WWE and their clinicians to ensure epilepsy and seizures are safely managed during pregnancy.

Several factors increase the frequency of seizures during pregnancy. Metabolic changes during pregnancy alter the pharmacokinetics of AEDs, increasing volume of distribution, renal clearance, and hepatic metabolism (9). Physiological changes during pregnancy, such as sodium retention and edema, can lead to HDP. These alterations can also increase brain irritability so that minimal sensory stimuli, including fatigue, nervousness, and emotional changes, can trigger seizures. In our study, 14.75% of pregnant WWE experienced HDP, and the incidence of seizures in pregnant WWE with hypertensive disorder was significantly higher than those without. The incidence of hypertension in pregnant women without seizures has been reported to be about 13.2% in a previous study (10).

These findings indicated that clinicians should make every effort to monitor and treat HDP in WWE. Neurologists and obstetricians should work together, taking a multidisciplinary approach to the management of pregnant WWE, to optimize pregnancy outcomes.

As this is a retrospective study, we could not confirm the causal relationship of hypertensive disorder and the incidence of seizures. A previous study has showed that neuropathological complications were associated with hypertensive disorders of pregnancy (11). Unfortunately, there are no reliable predictors of seizures during

pregnancy (2). Therefore, seizures should be controlled before pregnancy, and individualized therapeutic levels of AEDs should be established with monotherapy used where possible. WWE who are seizure-free in the 9 months prior to pregnancy have an 84–92% chance of remaining seizure-free during pregnancy on their current regimen (12). In our study, 52.46% of women remained seizure-free throughout pregnancy. These findings were consistent with previous studies that reported 58.3–66.6% of WWE participating in EURAP, the registry of international AEDs and pregnancy, were seizure-free throughout pregnancy (13,14). The risk of seizure during pregnancy corresponds to seizure type; WWE with complex partial seizures are more likely to experience seizures during pregnancy (15).

There were several limitations in this study. First, the sample size was not large enough to allow broad generalization of the results across different healthcare settings and regions. Second, we might have underestimated the proportion of pregnant WWE among the pregnant women attending the Beijing Tiantan Hospital, as cases may have been missed during screening. Third, the current study did not investigate the long-term outcomes of newborns. Fourth, brain images and EEGs were not performed in all patients to differentiate genetic and non-genetic epilepsies. Fifth, we did not set an internal control group to show the incidence of hypertension in pregnant women without seizures.

In conclusion, this study described the demographic and clinical characteristics of pregnant WWE, as well as the maternal and fetal outcomes. We found there were no significant differences in maternal or fetal variables, including age, median gestational age, gravidity, parity, incidence of seizures, mode of delivery or perinatal outcomes between pregnant women with a genetic and non-genetic basis for their epilepsy. The incidence of seizures was significantly higher in pregnant WWE with hypertensive disorder than those without. These data highlight the need that neurologists and obstetricians should work together to adopt a multidisciplinary approach to manage pregnant WWE in order to optimize pregnancy outcomes.

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### Footnote

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*Ethical Statement:* The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study conformed to the provisions of the Declaration of Helsinki (as revised in 2013). This study was approved Institutional Research Ethics Committee of Beijing Tiantan Hospital (No. KY 2019-029-02). Requirements for written informed consent were waived because all personal data were de-identified before the analyses.

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