



Epilepsy in China: Factors influencing marriage status and fertility

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ABSTRACT

Purpose: To investigate the current status of marriage and fertility of patients with epilepsy (PWE) and characterize its influencing factors.

Methods: A total of 1,823 adult patients (males age 22 years or older, females age 20 years or older) were included in this study. Data concerning sociodemographic and clinical characteristics were collected. Descriptive analyses, followed by univariate and multivariate logistic regression analyses were utilized to examine factors associated with marriage and fertility of PWE. Marital status of PWE was compared with Chinese population. Standardized marriage rate (SMR) for age and sex was estimated based on the 2010 sixth national population census.

Results: 1,132 patients (62.1%) were married and 823 (45.1%) had a history of fertility. Patients had lower marriage rates than Chinese population (62.1% vs 78.4%). Patients with adult-onset epilepsy (> 18 years) had a significantly higher rate of marriage and fertility ($p < 0.001$) compared to those with childhood-onset epilepsy (≤ 18 years). Employed patients had higher marriage rates than unemployed patients (64.9% vs 58.6%, $p = 0.006$), with only male patients being significantly affected by employment status ($p < 0.001$). Multiple logistic regression revealed that age, age at first seizure onset, and employment status were related to both marriage and fertility.

Conclusion: Epilepsy had negative effects on marriage and fertility status. Marriage and fertility rates were lower in patients with Childhood-onset epilepsy (≤ 18 years). Furthermore, employment status mainly affected the marriage rate of male patients.

1. Introduction

Epilepsy is a chronic disorder characterized by recurrent seizures affecting various aspects of social life [1,2]. It is generally agreed that patients with epilepsy (PWE) are less likely to get married and bear offspring [3–6]. Lower marriage rates and reduced fertility within marriage may be associated with sociological and clinical characteristics of epilepsy [5,7,8]. PWE have lower rates of marriage when disease onset in their first decade of life [3,5]. Carran et al. found that patients with temporal lobe epilepsy have higher marriage rates than those with extratemporal lobe epilepsy [5]. Patients with partial onset are more reproductively disadvantaged than those with generalized-onset seizures [8]. Meanwhile, a recent study has reported that there was no significant difference between single and married PWE in terms of seizure types and seizure frequency [9]. Other factors, including the

use of antiepileptic drugs (AEDs), may also contribute to reduced fertility among PWE [10,11]. AEDs treatment may affect the ability of PWE to conceive and increase the risk of abortion, and congenital malformations [8,12].

Marriage and fertility are central elements affecting the quality of life of PWE [2,13–15]. It is necessary to evaluate factors affecting marital and fertility status of PWE. Nevertheless, factors influencing marriage and fertility are controversial. There are few studies on this field of epilepsy from developing countries and relevant research in China is limited. Therefore, we conducted this study to investigate the current status of marital and fertility and its influencing factors.

Abbreviations: AEDs, antiepileptic drugs; PWE, patients with epilepsy; SMR, standardized marriage rate

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2. Materials and methods

2.1. Patients and procedures

Adult patients who came to our epilepsy outpatient clinic at West China Hospital between October 2013 and January 2017 were enrolled in this cross-sectional study based on an existing registry. A face-to-face interview with a semi-structured questionnaire was conducted in the outpatient clinic. Epilepsy was classified according to the new 2017 International League Against Epilepsy classification [16]. The inclusion criteria were as follows: (1) at least 1-year diagnosis of epilepsy, and (2) men aged 22 years or older and women aged 20 years or older (according to China's Marriage Law, men must be aged 22 years and women aged 20 years to get married).

The study was approved by the Ethics Committee of West China Hospital, Sichuan University. We informed all participants about the purpose of this study and obtained their written informed consent. The participants' confidentiality was guaranteed.

2.2. Data collection

Selected sociodemographic and clinical factors of the participants were collected in a semi-structured questionnaire, which included sociodemographic factors such as sex, age, residence (urban or rural), education, employment status, and marriage and fertility status. The collected clinical factors included age of first seizure onset, seizure type, temporal lobe epilepsy or not, number of antiepileptic drugs (AEDs), etiology of epilepsy. Marital status was defined as married (including a member of a married couple, divorced and widowed) and single (never married). This definition was recorded as a binary variable which is consistent with previous study [17]. Fertility was defined as reproduction of a new individual.

2.3. Data analysis

SPSS software (version 22.0, SPSS Inc., Chicago, Illinois, USA) was used for statistical analyses. First, data were entered into SPSS, and descriptive analyses were applied to dispose sociodemographic and epileptic clinical data, expressing results as percentages, mean, and standard deviation. Patients were categorized as being either (a) married or single, and (b) having fertility history (reproduced at least one child) or not. Standardized marriage rate (SMR) was calculated based on age-specific and sex-specific marriage rates in the sixth national population census. Marital status of PWE was compared with Chinese population (data from 2010 sixth national population census). Thereafter, univariate binary logistic regression analyses were used to examine differences by marital status and fertility. χ^2 tests were used for categorical data, and Mann-Whitney *U* tests were used for continuous data. Last, multivariate logistic regression analyses were conducted to select significant influential factors. Variables that yielded $P < 0.1$ in the univariate binary logistic regression were entered into a model of multivariable logistic regression. All P values were two-sided, with $P < .05$ considered as significant.

3. Results

On the basis of the inclusion criteria, 1,823 adult patients (females age 20 years or older and males age 22 years or older) were enrolled. Among these patients, 896 (49.1%) were male and 927 (50.9%) were female. A total of 1,132 patients (62.1%) got married, and 823 (45.1%) had a history of fertility. A total of 1567 (86.0%) patients with epilepsy graduated from secondary school level or higher. 1014 (55.6%) patients were employed. Etiology of epilepsy was classified as structural in 385 patients (21.1%) and non-structural in 1438 (78.9%). Demographic and clinical information regarding subjects are summarized in Table 1.

3.1. Marital status of the patients

Table 2 showed SMR of males/females, which was calculated by age and sex standardized method based on Chinese population of the 2010 sixth national population census. Marriage rates of PWE varied among the different age groups and increased with age. Among the 1,823 PWE, the marriage rate was 62.1%, while the SMR was 67.2%; with the SMR of female PWE being higher than male PWE. There was a difference between rural and urban regions in marriage rate for both national Chinese people (80.0% vs 74.9%) and patients with epilepsy (63.1% vs 61.6%). Although the marriage rate in rural area for both (people and patients) was higher than that in urban area, the marriage rate gap for PWE between urban and rural region has disappeared after standardization (67.5% vs 67.8%).

Patients had lower marriage rates than the Chinese population (data from 2010 sixth national population census). PWE older than 50 years remained married as often as the national population (Fig. 1a and Table 3). Fig. 1b shows that 91.5% PWE older than 50 years got married before the first seizure onset. Furthermore, female patients but not male patients contributed to decreased marriage rate (Fig. 1c and d).

For PWE and national Chinese under 25 years old, marriage rate in rural region was higher than urban region regardless of epilepsy. Marriage rate of PWE grew slower than national Chinese between 25 and 50 years old. But the negative influence of epilepsy disappeared between PWE and national Chinese older than 50 years old (Fig. 2).

In the univariate analysis, employed patients had higher marriage rates than unemployed patients (64.9% vs 58.6%, $p = 0.006$) (Table 1). 367 (68.0%) of 540 employed male patients got married, and only 196 (55.1%) of 356 unemployed male patients did so (55.1% vs 68.0%, $p < 0.001$). Nevertheless, the marriage rate of female patients was not influenced by employment status (61.4% vs 61.4%, $p = 0.994$) (Table 4). Patients with onset of epilepsy at the age of ≤ 18 years were less likely to get married compared to patients with epilepsy onset after the age of 18 years (42.2% vs 76.9%, $p < 0.001$). But there was no difference in marriage rate among the different age groups of patients with seizure onset before 18 years old (Table 1 and Fig. 3). Marital status differed significantly by other factors such as age of patients, education level, and the number of AEDs. There was no difference in marriage rate based on sex, seizure types, temporal lobe epilepsy and etiology of epilepsy (Table 1).

Logistic regression was used to determine the factors that potentially affect marital and fertility status. Age of patient, employment status, education level, age of first seizure onset and number of AEDs were included in the model of marriage. Multiple logistic regression has revealed that age ($B = -1.541$, $P < 0.001$), employment status ($B = -0.261$, $P = 0.031$), and age at first seizure onset ($B = -0.722$, $P < 0.001$) were the independent variables that affect marital status (Table 5).

3.2. Fertility status in Chinese PWE

Table 1 shows that males with epilepsy have higher rate of fertility than females (48.5% vs 41.8%, $p = 0.004$). Patients with onset of epilepsy at the age of ≤ 18 years old had a lower rate of fertility (25.4% vs 59.8%, $p < 0.001$) (Table 1). Fertility status differed significantly by other factors such as sex, age of patient, education level and employment status. The mean number of children in female PWE was lower than the female national Chinese (Fig. 4).

Age, sex, education level, employment status, and age of first seizure onset were included in the model of fertility. Multiple logistic regression has revealed that age ($B = 1.090$, $P = < 0.001$), age at first seizure onset ($B = 0.787$, $p = < 0.001$), employment status ($B = 0.408$, $P = 0.001$) and education level ($B = -0.418$, $p = < 0.001$) were the independent variables that affect fertility status (Table 5).

Table 1
Demographic and clinical variables.

Variables	Marriage			Fertility ^a		
	Married PWE	Single PWE	<i>p</i>	Yes	No	<i>p</i>
Total	1132 (62.1%)	691 (37.9%)		823 (45.1%)	1000(54.9%)	
Sex			0.522			0.004*
Female	569 (61.4%)	358 (38.6%)		388 (41.8%)	539(58.1%)	
Male	563 (62.8%)	333 (37.2%)		435 (48.5%)	461(51.5%)	
Median age, Q25/Q75 (years)	37 (29/47)	24 (22/27)	–	40 (31/49)	26 (23/30)	–
Age range (years)			< 0.001*			< 0.001*
20–29	323 (35.5%)	587 (64.5%)		164 (18.0%)	746(82.0%)	
30–39	316 (80.8%)	75 (19.2%)		239 (61.1%)	152(38.9%)	
40–49	268 (91.2%)	26 (8.8%)		228 (77.5%)	66(22.4%)	
50–	225 (98.7%)	3 (1.3%)		192 (84.2%)	36(15.8%)	
Residence			0.551			0.204
Rural	379 (63.1%)	222 (36.9%)		284 (47.2%)	317(52.7%)	
urban	753 (61.6%)	469 (38.4%)		539 (44.1%)	683(55.9%)	
Education			< 0.001*			< 0.001*
Primary school or lower	168 (65.6%)	88 (34.4%)		132 (51.5%)	124(48.4%)	
Secondary school	603 (66.7%)	301 (33.3%)		479 (53.0%)	425(47.0%)	
University or above	361 (54.4%)	302 (45.6%)		212 (32.0%)	451(68.0%)	
Employment status			0.006*			0.028*
Not employed	474 (58.6%)	335 (41.4%)		342 (42.3%)	467(57.7%)	
Employed	658 (64.9%)	356 (35.1%)		481 (47.4%)	533(52.6%)	
Median age of first seizure onset, Q25/Q75 (years)	26 (17/38)	16 (11/21)	–	29 (19/40)	17 (12/22)	–
Age of first seizure onset			< 0.001*			< 0.001*
> 18 years	804 (76.9%)	242 (23.1%)		626 (59.8%)	420 (40.2%)	
≤ 18 years	328 (42.2%)	449 (57.8%)		197 (25.4%)	580 (74.6%)	
Seizure type-Focal seizure	754 (61.8%)	467 (38.2%)	0.667	557 (45.6%)	664 (54.4%)	0.563
Temporal lobe epilepsy	253 (58.7%)	178 (41.3%)	0.096	183 (42.5%)	248 (57.5%)	0.200
Number of AEDs-polytherapy	519 (59.5%)	353 (40.5%)	0.030*	388 (44.5%)	484 (55.5%)	0.593
Etiology-structure	246 (63.9%)	139 (36.1%)	0.412	177 (46.0%)	208 (54.0%)	0.713

Abbreviation: PWE, patients with epilepsy; AEDs, antiepileptic drugs.

^a Patients with at least one liveborn offspring.* *p* < 0.05.**Table 2**
Standard marriage rate (SMR^a) of PWE, marriage rate of PWE and national Chinese.^b

Variables	SMR ^a (%)	Marriage rate of PWE (%)	Marriage rate of national Chinese ^b (%)	<i>X</i> ²	<i>P</i>
Gender					
Male	62.8	62.8	75.3	32.192	< 0.001*
Female	69.5	61.4	81.5	80.840	< 0.001*
Residence					
Rural	67.8	63.1	80.0	17.896	< 0.001*
Urban	67.5	61.6	74.9	12.393	< 0.001*
Total	67.2	62.1	78.4	57.068	< 0.001*

Abbreviation: PWE, patients with epilepsy; SMR, standard marriage rate of PWE.

^a SMR was calculated on the basis of age-specific marriage rates in the Chinese people of the 2010 sixth national population census.^b Marriage rate of national Chinese is according the data obtained from the sixth national population census (2010).* *p* < 0.05.

4. Discussion

Patients with epilepsy experience decreased fertility and marriage rate compared to people in national [3,8,18,19]. The marriage rate for PWE varies across different countries [3,5,13,20,21]. Negative public attitudes toward PWE persist, regardless of ethnicity, culture, or country [22]. The marriage rate in this sample was 62.1% and the SMR was 67.2%. Marriage rate rose after standardization, which indicates that the age composition of this sample was younger than that of the national population. Besides, over 90% of patients older than 50 years got married before the first seizure onset, while this proportion is much higher than young PWE which might explain why PWE older than 50

years got married as often as national Chinese.

Previous studies have generally shown a lower rate of marriage for male PWE compared with female PWE [3,5]. Likewise, we found that female PWE have a higher SMR than male PWE after age and sex standardization. This result suggests that the age composition of the female population in this sample was younger than that of the national population, whereas that of the male population was similar to national Chinese. In the present study, we also found that there is no difference in marriage rate between patients with epilepsy living in urban and rural regions, suggesting that epilepsy itself has bigger impact on marriage rate than marriage gap between urban and rural region.

Sociologic factors including age, education, and employment status have a close relationship with marital status [1,2,9]. For general public, men and women are more likely to marry when they are employed [23]. Both men's and women's economic resources are positively related to marriage, but men's economic resources are more strongly related to marriage than women's [23]. In the present study, married adult patients demonstrated a higher employment rate than unmarried patients; this finding is consistent with a previous study from China [2]. Compared with female PWE, unemployed male patients were more likely to be single. Wada et al. also found a significant difference in marriage rates between the employed and unemployed male patients, which suggests that having a job is an important factor for marriage in males [1]. Occupation status probably affects men more, because women are traditionally seen as homemakers and allowed to be financially dependent on their spouses. Men with good economic resources represented by their ability to afford marriage make them more attractive as potential companion [23]. Thus there is a different level of expectation from males regarding social and financial independence [5].

We have found that early age of onset of epilepsy was associated with reduced rates of marriage and fertility. Studies from developed

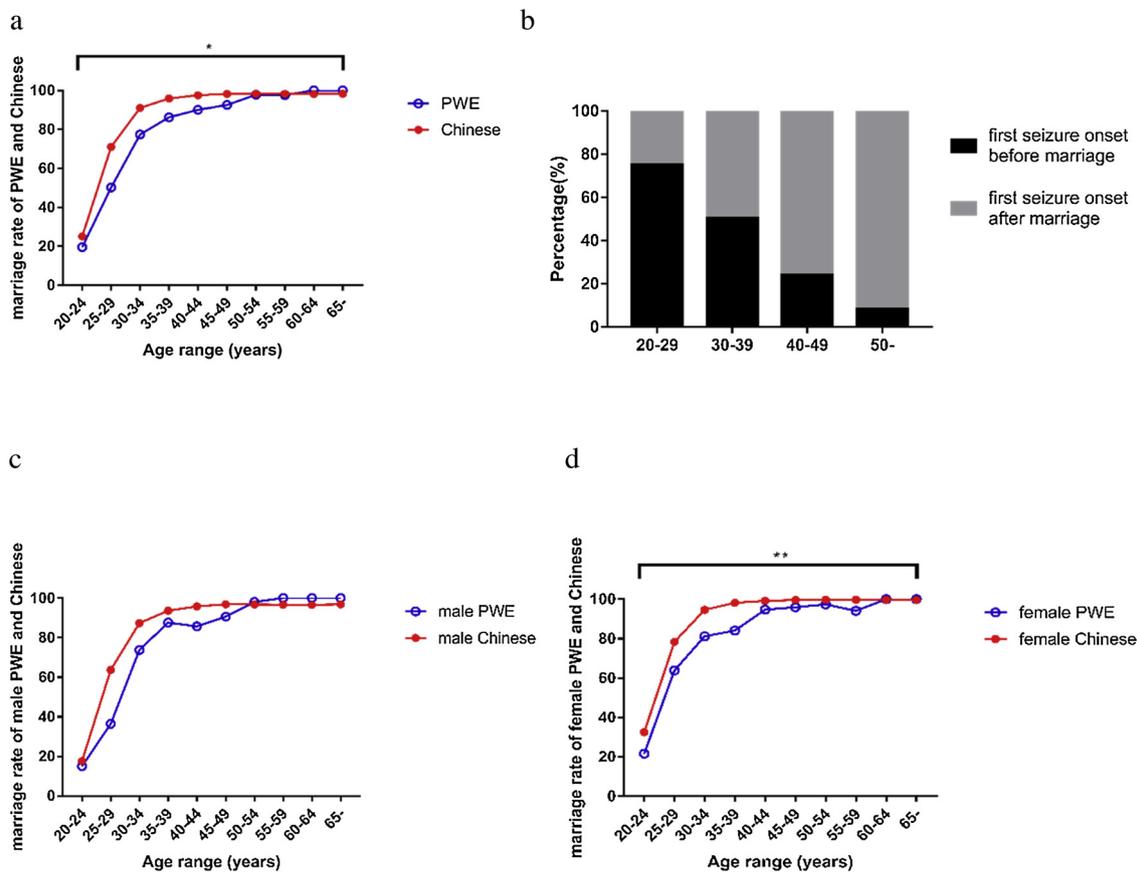


Fig. 1. a) Comparison marriage rate of PWE and national Chinese population. b) Proportion of PWE with the first onset of seizure before marriage and after marriage. c) Comparison marriage rate of male PWE and national male Chinese. d) Comparison marriage rate of female PWE and national female Chinese. * $p < 0.05$. ** $p < 0.005$.

Table 3
Comparison of marriage rate of PWE and national Chinese.^a

Age range (years)	Marriage rate of PWE (%)	Marriage rate of national Chinese ^a (%)	χ^2	P
20–24	19.5	25.0	3.819	0.051
25–29	50.2	71.1	43.321	< 0.001*
30–34	77.4	91.0	16.021	< 0.001*
35–39	86.2	95.9	9.146	0.002 [†]
40–44	90.0	97.5	7.680	0.006 [†]
45–49	92.5	98.2	5.583	0.018 [†]
50–54	97.8	98.2	–	– ^b
55–59	97.6	98.2	–	– ^b
60–64	100.0	98.1	–	– ^b
65–	100.0	98.3	–	– ^b

Abbreviation: PWE, patients with epilepsy.

^a Marriage rate of national Chinese is according the data obtained from the sixth national population census (2010).

^b $p > 0.1$.

* $p < 0.05$.

and developing countries have shown a similar finding of decreased marriage or fertility rates in patients with earlier age of seizure onset [18,22,24,25]. PWE with an early age of seizure onset may be over-protected, which leads to independent social functioning deficiency [5]. This social maladjustment may be due to specific medical, social, psychological problems or discrimination caused by long-term illness. Patients with childhood-onset epilepsy have a higher rate of psychiatric and psychosomatic disorders; moreover, long-term AED therapy may affect employment and driving [26]. These patients may be unable to take their social and economic obligations.

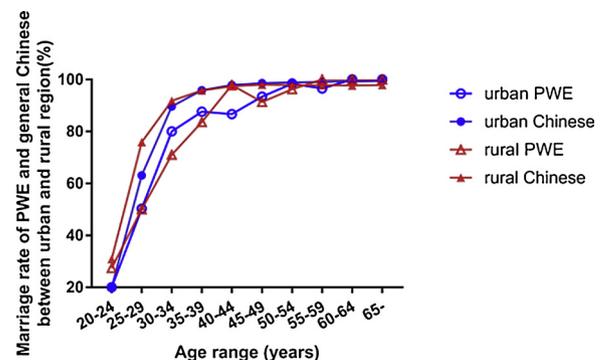


Fig. 2. Comparison marriage rate of PWE and national Chinese of different living area.

Table 4
Comparison of marital status for PWE with different employment status.

	Married	Single	OR	p
Male (n,%)			0.577(0.438–0.761)	< 0.001 [†]
Employment	367(68.0)	173 (32.0)	1.255(1.113–1.414)	
Unemployment	196(55.1)	160 (44.9)	0.725(0.618–0.849)	
Female (n,%)			0.999(0.767–1.301)	0.994
Employment	291(61.4)	183(38.6)	1.000(0.879–1.139)	
Unemployment	278(61.4)	175(38.6)	.999(0.873–1.144)	

Abbreviation: PWE, patients with epilepsy.

* $p < 0.05$.

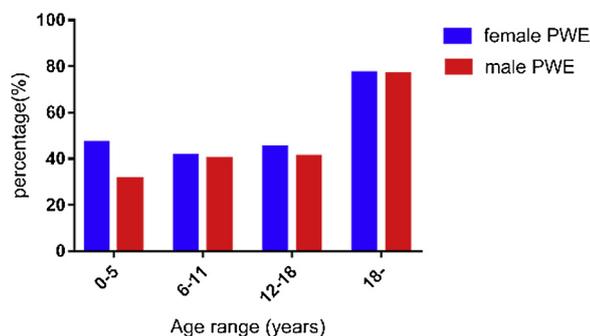


Fig. 3. Comparison between marriage and fertility rates of different age of first seizure onset.

In the present study, there was no difference in marriage rate based on seizure types, temporal lobe epilepsy and etiology of epilepsy. Wada et al. found that seizures were not controlled in many PWE when they were married, which suggests that seizures themselves may not markedly inhibit marriage [1]. Factors such as seizure types and etiology of epilepsy did not appear to exert a negative influence on current marital status, which is consistent with other studies [9,13,22]. Carran et al. found that the patients with temporal lobe epilepsy are more likely to be married than those with extratemporal epilepsy, which may be ascribed to limbic system dysfunction [5]. However, this hypothesis was not supported by our data; we found that there is no difference between patients with temporal lobe epilepsy and patients with extratemporal lobe epilepsy in terms of marriage status. This might be caused by different inclusion criteria. In the study of Carran et al [5], all patients with medically refractory epilepsy were included and most of them (346/430) were diagnosed with temporal lobe epilepsy. Further studies are needed to explain this interesting point: whether marital status of PWE is influenced by temporal epilepsy.

PWE have a lower rate of fertility this might be attributed to a decreased marriage rate [8,25]. We found that female PWE have fewer children than female national population. Moreover, Female PWE had lower rates of fertility than male PWE (48.5% of male, 41.8% of female, $p = 0.004$). A significantly large population-based cohort study including over 1.4 million singleton births has revealed that epilepsy during pregnancy is associated with increased risks of adverse pregnancy and perinatal outcomes [27]. Married female patients more commonly experience therapeutic abortions than male patients' healthy wives [3]. Patients with epilepsy receiving AEDs had fewer children [25]. AEDs treatment may affect the ability of female PWE to conceive, increase the risk of abortion, and impact sexual and neuroendocrine function [8]. The combination of more than three drugs has increased the risk of major congenital malformations [12]. Recent studies revealed that AEDs such as valproate, phenobarbital, and carbamazepine have dose-dependent increased risk of congenital malformations

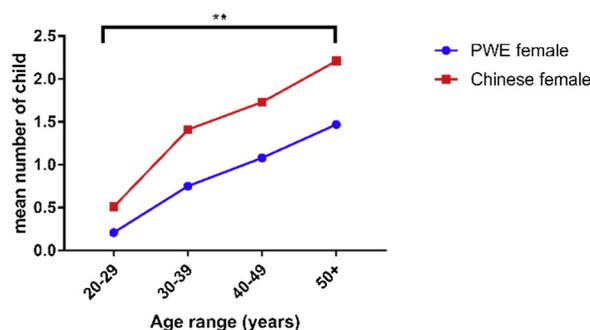


Fig. 4. Comparison between the mean number of new individuals of female PWE and female national Chinese.

** $p < 0.005$.

[12,28]. A daily dose of AEDs greater than a certain minimal level is likely to produce malformed infants [29]. Moreover, AEDs and AEDs-induced androgen deficiency could also attribute to diminished libido and sexual dysfunction among male epileptic patients [30].

Traditional concept such as fear of having a child with epilepsy also influences the decision of reproduction [18]. Our previous study showed that 11.8% Chinese patients with epilepsy are concerned about the heritability of seizure [31]. Discrimination against PWE exists in different ethnicity, culture, or country [22,32,33]. Many studies have revealed that some families still disagree that their children should marry PWE, because they are afraid that PWE will pass the illness to their descendants [3]. Thabit et al. designed a study to assess the attitudes toward patients with epilepsy, and found that approximately 49.9% of individuals without epilepsy are not able to marry a partner with epilepsy, and 49.9% of them think that PWE should not have children [34]. In Korea, most people still have negative attitudes toward epilepsy because they think that "epilepsy cannot be treated [32]. Social stigmatization of epilepsy and perceived stigma of patients both have effect on the marital status of PWE [22].

Several limitations should be noted in this study. First, the study was cross-sectional and non-randomized, and this impedes accuracy of determining status and influenced factors of marriage and fertility. Second, PWE were recruited from a tertiary referral center and this setting may introduce some selection bias. According to our definition, divorced and widowed people were defined as "married" both in patients and national Chinese, which may subtly affect the marital status. In addition, because it is usually not socially acceptable to openly discuss marital problems in Chinese culture [13], data on demographic and clinical information in this sample were based on self-report and prone to responder bias. Further studies on multicenter and cross-cultural comparison are needed.

Table 5
The potential contributing factors affecting the status of marriage and fertility^b in Chinese PWE.

Variable ^a	Logistic regression, multivariate							
	Marriage				Fertility ^b			
	B	Exp(B)	95%CI	p-value	B	Exp(B)	95%CI	p-value
Age	-1.541	0.214	0.178–0.259	<0.001	1.090	2.975	2.615–3.386	<0.001
Employment	-0.261	0.770	0.608–0.976	0.031	0.408	1.504	1.190–1.902	0.001
Age of first seizure onset	-0.722	0.486	0.383–0.617	<0.001	0.787	2.196	1.728–2.791	<0.001
Education	-	-	-	-	-0.418	0.659	0.553–0.784	<0.001

Abbreviation: AEDs, antiepileptic drugs; PWE, patients with epilepsy.

^a Age range, employment, education, temporal lobe epilepsy, age of first seizure onset and number of AEDs were entered into model of marriage. Age range, gender, employment, education and age of first seizure onset were entered into model of fertility. Only significantly associated factors were listed in this table.

^b Patients with at least one liveborn offspring.

5. Conclusion

Epilepsy had a negative effect on marriage and fertility. PWE with early age of seizure onset (younger than 18 years old) were less likely to get married. Employment status mainly affected the marriage rate of male patients. The type of seizure, temporal lobe epilepsy and etiology did not have any effect on marriage and fertility status. Therefore, children PWE should be early diagnosed, properly treated and provided with psychological intervention when needed. Female PWE are supposed to seek consultations when they get pregnant or considering pregnancy. Improving employment policy and foster institutional guarantee for employment will positively influence the marital status of PWE, especially in male patients. Moreover, greater concerted public efforts are needed to create a better environment in which PWE can be understood and supported.

Declaration of Competing Interest

There are no known conflicts of interest associated with this publication and there has been no significant financial support for this work that could have influenced its outcome.

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