



FULL-LENGTH ORIGINAL RESEARCH

An epidemiological survey of epilepsy in tropical rural areas of China

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Abstract

Objective: Epilepsy is a chronic neurological disease that is characterized by seizures. Seizure episodes, stigma, and high medical costs associated with this condition caused significant psychological distress. This study aimed to evaluate epidemiological characteristics and treatment status of epilepsy in individuals existing in the tropical rural areas of Hainan Province of China.

Methods: A household survey on epilepsy was conducted among the rural population of Chengmai County, Danzhou City, Baoting Autonomous County (Li and Miao nationalities), and Dangan County in Hainan Province, China. A screening questionnaire based on the standard screening questionnaires of the World Health Organization (WHO) was designed and a screening instrument of International Community-based Epilepsy Research Group was used. Individuals suspected or previously diagnosed with epilepsy were reexamined by an experienced neurologist. Further clinical data were collected from subjects with confirmed diagnosis of epilepsy.

Results: This study included 16 676 subjects with 8827 men (52.93%) and 7849 women (47.07%). Majority of the study subjects included were of Han Chinese (N = 13 145, 78.83%), and the remaining were of Li minority ethnicity. The incidence of epilepsy was 0.24 per 1000, and the total prevalence of active epilepsy was 2.33 per 1000. The prevalence of epilepsy in the Han and Li nationalities was 3.27 and 2.27 per 1000, respectively, which was shown to be higher in people aged ≥ 60 . The initial onset of epilepsy tended to trigger among children aged between 0 and 9 years old. Initial assessment revealed that the treatment gap for active epilepsy was 58.97%, and stroke is shown as the most common cause of symptomatic epilepsy.

Significance: The prevalence and incidence of epilepsy in tropical rural areas of Hainan Province were close to those of the earlier findings that are reported in other regions of China and lower than those remaining in the tropical areas around the

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world. There exists a huge treatment gap for active epilepsy, which indicates an urgent need for a rational intervention strategy.

KEYWORDS

epidemiology, epilepsy, Hainan Province, treatment gap, tropical areas

1 | INTRODUCTION

Epilepsy is a chronic disease that is characterized by transient brain dysfunction causing seizures.^{1,2} Seizures, discrimination, and medical costs bring psychological distress to patients and their families, worrying about employment and work ability.^{3,4} Epilepsy is a serious medical and social problem that has a profound impact on the quality of life of both patients as well as their relatives. The distribution and treatment status of epilepsy have been the main research focus throughout the world, and these data have become fundamental for disease prevention as well as treatment. According to the World Health Organization (WHO) report, epilepsy is more common in developing countries than in developed countries, accounting for a prevalence of 6.1‰ and 5.0‰, respectively.^{1,2} More than 80% of the global burden of epilepsy is involved in poverty-stricken regions of developing countries. There are fairly a large number of epileptics who are unable to obtain treatment, particularly in rural locations. Epilepsy is estimated to have affected up to 9 000 000 people in China, and a treatment gap of 63% has been reported in rural areas.^{5,6} The rural population in China has low literacy levels and limited knowledge with regard to epilepsy, and therefore, the symptoms of onset, including sudden falls, convulsions, and foaming from the mouth, might lead to misunderstanding and fear among the observers. These characteristics make rural patients more susceptible to prejudice, discrimination, and alienation.⁷

The incidence of epilepsy is higher in tropical regions than other regions, which might be due to poor sanitary conditions and greater risk of parasitic infections. Although several epidemiological investigations on epilepsy have been carried out in China since 1980,⁸ there were only few studies reported on the epidemiological characteristics of epilepsy in Hainan Province, which is the only tropical region of China.^{9,10} Therefore, an epidemiological investigation was conducted from December 2016 to November 2017 in some villages of Chengmai County, Danzhou City, Dingan County and Baoting Autonomous County (Li and Miao nationalities) in the Hainan Province.

2 | METHODS

2.1 | Study areas and population

This study was conducted in Hainan, which is the largest special economic zone and the only tropical island province

Key points

- The total prevalence of epilepsy in tropical rural areas of China (Hainan Province) was 3.06‰ and the incidence rate was 23.99 per 100 000
- The incidence of epilepsy was higher in men than in women and the onset of epilepsy was relatively higher in 0-9 years age group
- The two leading causes of epilepsy in Hainan Province are stroke and encephalitis, and generalized epilepsy was more commonly seen

that is dominated by tropical forests in China with approximately 8 671 500 inhabitants according to the Sixth National Population Census. This study was conducted in four cities of Hainan: Chengmai County (483 900 inhabitants) in the north, Danzhou City (977 700 inhabitants) in the northwest, Baoting Autonomous County (Li and Miao nationalities) (150 200 inhabitants) in the south-central, and Dingan County (291 400 inhabitants) in the northeast. The minority groups living in this province were the Li and the Miao.

2.2 | Sampling

The rural areas in these four cities were randomly selected by multistage cluster sampling (Figure 1 marked by red). Firstly, a township was initially selected from each city through simple random sampling, and then 6 to 12 villages were selected in each township according to the presence of population size. Residents of all age groups were incorporated in this study. Finally, a total of 16 676 residents were included in our study.

2.3 | Operational and diagnostic criteria

The criteria of International League Against Epilepsy (ILAE) 2014¹¹ were used for diagnosing epilepsy, which included the occurrence of at least two unprovoked (or reflex) seizures with >24 hours apart; one unprovoked (or reflex) seizure and the risk of additional seizures that are similar to the overall risk of recurrence (at least 60%) after two unprovoked seizures in the next 10 years; and diagnosis of epileptic syndrome. The

FIGURE 1 ● Townships initially selected from each city through simple random sampling were marked in red. 6 to 12 natural villages are extracted from each township and included subjects were all ages who had permanent household registration and lived locally



seizures triggered during the acute phase of central nervous system diseases were not considered as epileptogenic in origin.

The occurrence of spontaneous seizures more than twice on different dates in the past year leads to the diagnosis of active epilepsy.

The prevalence rate here refers to the proportion of all new as well as preexisting (regardless of when the illness has begun) epilepsy in individuals interviewed during our study.

Incidence in this study refers particularly with regard to the incidence proportion (risk), namely the occurrence of new cases of epilepsy during the observation period. As a measure of incidence, it includes only new cases identified during the period of observation in the numerator and the “population at risk” for developing epilepsy during the start of our research in the denominator.

Classification of seizures: According to the “Commission on Classification and Terminology of the International League Against Epilepsy” published in 2010, epileptic seizures were classified into three types as focal, generalized, and unclassified.¹²

Treatment status: The treatment status in this survey was divided into 3 categories as regular, irregular, and untreated. Regular treatment means standard treatment with antiepileptic drugs regularly. Irregular treatment includes traditional Chinese medicine, folk prescription, and inappropriate treatment.¹³

Epileptic treatment gap: The percentage of people without regular treatment in a given population at a given time.¹⁴

2.4 | Study design and procedure

The study design involved preliminary screening followed by reexamination. Household surveys were conducted by trained and qualified examiners (one medical resident or two medical

graduate students). The survey respondents who signed the informed consent form were invited to fill in a screening questionnaire, which comprised of 13 questions established by the WHO in 2000.¹⁵ Data of the participants who are away from home during initial screening due to farming activities were provided by the family members or attending physicians. An experienced neurologist examines the respondents with suspected or confirmed epilepsy for a definitive diagnosis and filled out a registration form for epilepsy cases. Before conducting the formal survey, information about epilepsy and clinical pilot studies were provided.

2.5 | Statistical analysis

All data collected were transferred into an Excel worksheet and analyzed using SPSS software, version 20.0 (IBM Corp). The prevalence rate was determined by dividing the number of observed epilepsy cases by the total number of screened cases. The incidence rate was defined as the frequency of patients newly diagnosed with epilepsy as compared to those without epilepsy before. Descriptive statistics such as frequency, means, and standard deviation were calculated for baseline demographic characteristics. Intergroup differences in categorical variables were analyzed by chi-square test. Alternatively, Fisher's exact probability was computed when the data is unconformable for certain conditions of chi-square test. Both point estimation and 95% confidence interval for prevalence and incidence were calculated.

2.6 | Ethical considerations

This study was approved by the Research Ethics Committee of the First Affiliated Hospital of the Hainan Medical

University. All subjects have provided signed informed consent to participate in this study.

3 | RESULTS

3.1 | Demographic characteristics

According to the most recent census in 2010, a total of 1 903 200 individuals from 4 sites were included in our survey. A total of 16 676 individuals included in our study were distributed as follows: Chengmai (N = 2750), Danzhou (N = 5301), Baoting (N = 3531), and Dingan (N = 5094), (Table 1). In this sample, the Han nationality population is the largest of the ethnic groups with 13 145 and then Li nationality with 3531. A total of 16 676 residents were evaluated, and the response rate of the household survey and interview was 98% and 90%, respectively.

3.2 | Prevalence of epilepsy

The overall prevalence of epilepsy in Hainan Province was 3.06%, and the standardized prevalence rate was 4.87% based on the Sixth Population Census (2010) demographic structure. The prevalence rate of epilepsy in Chengmai County was comparatively higher (4.00%, 95% CI 1.64-6.35), and the prevalence rate of epilepsy in Baoting County was relatively lower (2.27%, 95% CI 0.70-3.83). The prevalence rate of epilepsy in men (3.29%, 95% CI 2.09-4.48) showed no significant differences ($P = .317$) when compared to women (2.80%, 95% CI 1.63-3.97). The prevalence rate of epilepsy in both Han and Li nationalities was 3.27% (95% CI 2.30-4.25) and 2.27% (95% CI 0.70-3.83), respectively, and the difference showed no significant difference (Table 2).

3.3 | Prevalence and incidence of active epilepsy

This study analyzed only the epileptic episodes that occurred before and during the study. The overall prevalence of active

epilepsy with seizures was 2.33‰ (95% CI 1.61-3.19), and the prevalence rate of active epilepsy was comparatively higher in Chengmai County (3.27‰, 95% CI 1.14-5.41) and relatively lower in Baoting County (1.42‰, 95% CI 0.18-2.66) with no significant differences ($P = .88 > .05$). The overall incidence of epilepsy in the four locations was 23.99 per 100 000 (95% CI 0.005-0.94), and their respective incidence was shown in Table 2.

3.4 | First onset of epilepsy in different age groups

The prevalence of epilepsy was increased with increasing age (Figure 2A) and reached peak in age groups 20-29 and ≥ 60 years. The first onset of epilepsy tends to occur in 0-9 years of age (Figure 2B).

3.5 | Causes of symptomatic epilepsy and types of epilepsy

A total of 15 patients presented symptomatic epilepsy. The most common causes of epilepsy included stroke (5 cases, 9.80%) and encephalitis (5 cases, 9.80%), followed by hypoxia (1 case, 1.96%) and head trauma (1 case, 1.96%). Generalized seizures were more commonly observed, accounting for 68.63% (35 cases) of the cases. Focal seizures accounted for 29.41% (15 cases) and unidentifiable (1 case) accounted for 1.96%.

Among the active epileptic patients who still had seizures within 1 year, only 41.03% received conventional antiepileptic treatment within 1 week before the survey. The treatment gap between seizure recurrences was 58.97% (Table 3).

4 | DISCUSSION

4.1 | Prevalence and Incidence rate

The mean rate of epilepsy in developed countries and rural areas of developing countries is 5.8‰ and 15.4‰, respectively.² The prevalence rate of epilepsy in sub-Saharan Africa

TABLE 1 Baseline demographic characteristics of the study population

Region	Population	Sample size	Case gender		Age (years)							Nationality	
			Male	Female	0-9	10-19	20-29	30-39	40-49	50-59	≥ 60	Li	Han
Chengmai	483 900	2750	7	4	148	299	539	548	393	357	466	0	2750
Danzhou	977 700	5301	10	6	437	951	1295	1008	673	447	490	0	5301
Baoting	150 200	3531	4	4	536	385	581	681	511	439	398	3531	0
Dingan	291 400	5094	8	8	812	778	1002	809	540	473	680	0	5094
Total	1 903 200	16 676	29	22	1933	2413	3417	3046	2117	1716	2034	3531	13 145

TABLE 2 Epidemiology characteristics of epilepsy in rural Hainan

Region	Sample size	Number of cases	Number of new cases	Cases with regular treatment	Cases with active epilepsy	Incidence of epilepsy (%) ^a	Prevalence of epilepsy (%) ^a	Prevalence of active epilepsy (%) ^a	Treatment gap (%)
Chengmai County	2750	11	0	3	9	0.00 (0.00, 0.00)	4.00 (1.64, 6.35)	3.27 (1.14, 5.41)	66.67
Danzhou County	5301	16	1	6	13	0.19 (-0.18, 0.56)	3.02 (1.54, 4.50)	2.45 (1.12, 3.78)	53.85
Baoting County	3531	8	1	3	5	0.28 (-0.27, 0.84)	2.27 (0.70, 3.83)	1.42 (0.18, 2.66)	40.00
Dingan County	5094	16	2	4	12	0.39 (-0.15, 0.94)	3.14 (1.60, 4.68)	2.36 (1.02, 3.69)	66.67
Total	16 676	51	4	16	39	0.24 (0.005, 0.94)	3.06 (2.22, 3.90)	2.33 (1.61, 3.19)	58.97
χ^2 (P) ^c						0.84 ^b	1.54 (0.67)	0.75 ^b	0.86 ^b

^aData with both point estimate and 95% confidence intervals.

^bP value of Fisher's exact test.

^cComparison between four studied rural areas.

and Latin America (15% and 17.8%, respectively) was higher than that in Asia and Europe/North America (6.0%, and 8.0%, respectively).¹⁶ The overall prevalence of epilepsy in China ranged from 1.43% to 8.51%, and the mean rate was 7.0%.¹⁷ The results of the present study showed that the total prevalence of epilepsy in rural areas of Hainan Province was 3.06% (95% CI 2.22-3.90), and the standardized prevalence was 4.87%, which was obviously lower than the results obtained from other tropical regions and similar to nontropical areas in China.

The incidence of epilepsy in developed countries and low/middle-income countries is 45 per 100 000 and 81.7 per 100 000, respectively.¹⁸ Studies have found that the incidence of epilepsy in low-income countries in South Africa ranged from 180 to 250 per 100 000.⁹ A study conducted in 2000 showed that the total annual incidence of epilepsy in China was 28.8/100 000.⁹ The present findings indicated that the incidence of epilepsy in the rural areas of Hainan Province was 0.24 per 1000, which is similar to the results of the previous epidemiological surveys conducted in other regions of China.^{19,20}

4.2 | Gender and nationality

Agreement on the differences in epilepsy prevalence between gender has yet to be investigated, and the prevalence of epilepsy in both men and women in China was different from that reported in other countries. Though previous studies have demonstrated that the prevalence of epilepsy was higher in men than those in women of Russia and Spain,^{21,22} an epidemiological survey conducted in five provinces of China showed that the prevalence of epilepsy was higher in women than in men.²³ The results of the present study reported that the prevalence of epilepsy was higher in men (3.29%, 95%CI 2.09-4.48) than in women (2.80%, 95%CI 1.63-3.97), which was in agreement with the epidemiological surveys conducted abroad. The prevalence of epilepsy in Li nationality (2.27%, 95%CI 0.70-3.83) was lower than that in Han nationality (3.27%, 95%CI 2.30-4.25), which might be due to the differences between ethnic groups in China. However, chi-square test demonstrated no significant differences in this parameter between these two groups and genders. Moreover, the number of respondents from Li group was small, causing information bias (Table 3).

4.3 | Onset of epilepsy in different age groups

The relationship between the prevalence rate and age at onset of epilepsy also varied among different studies conducted in China and elsewhere. A study conducted in Benin found that the prevalence of epilepsy in age group of 20-49 was

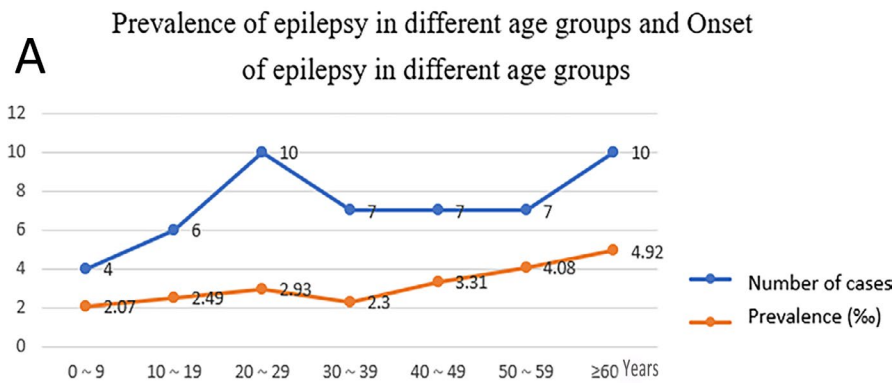


FIGURE 2 The prevalence of epilepsy was increased with increasing age (A) and reached peak in age groups 20-29 and ≥ 60 y. The first onset of epilepsy tends to occur in 0-9 y of age (B)

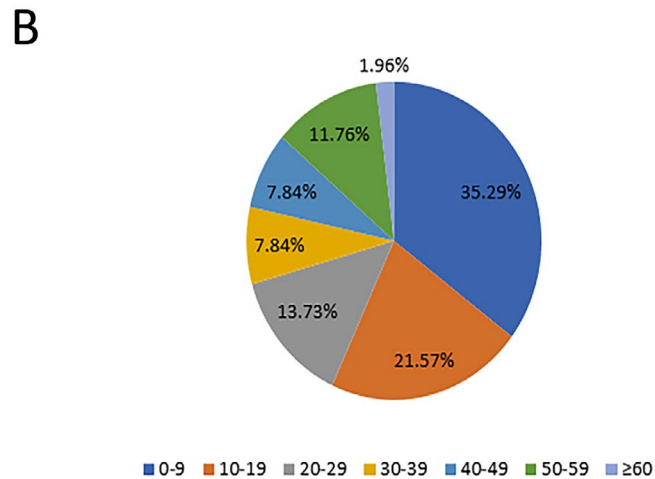


TABLE 3 Gender differences and racial differences of epilepsy epidemiology characteristics in rural Hainan

Group	Sample size	Number of cases	Cases with active epilepsy	Prevalence of epilepsy (%) ^a	χ^2 (P)	Prevalence of active epilepsy (%) ^a	χ^2 (P)
Gender							
Male	8827	29	22	3.29 (2.09, 4.48)	0.31 (0.57)	2.49 (1.45, 3.53)	0.11 (0.746)
Female	7849	22	17	2.80 (1.63, 3.97)		2.17 (1.14, 3.19)	
Nationality							
Li	3531	8	5	2.27 (0.70, 3.83)	0.92 (0.34)	1.42 (0.18, 2.66)	0.20 ^b
Han	13 145	43	34	3.27 (2.30, 4.25)		2.59 (1.72, 3.46)	

^aData with both point estimate and 95% confidence intervals.

^bP value of Fisher's exact test.

significantly higher than that in childhood.²⁴ Nonetheless, the findings of the present study indicated that this rate was comparatively higher in people who are 60 years or older, and this might be related to age stratification in the survey area. According to a survey conducted in Kenya, the incidence of epilepsy was relatively higher in 6-17 age group and is comparatively lower in the 28-49 age group. In addition, the incidence of epilepsy is reported to be increased in people aged more than 50.²⁵ A meta-analysis conducted in India reported that the onset of epilepsy reached peak in subjects aged between 10 and 19 years,²⁶ and an epidemiological survey conducted in five provinces of China demonstrated that the onset of epilepsy is more common in children aged between 0 and

9 years, and this is rarely seen in older age groups.²³ Other studies conducted in China found that the onset of epilepsy is comparatively higher in individuals of 0-9 age group.^{23,27,28} Similarly, our results indicated that the onset of epilepsy was relatively higher in individuals of 0-9 age group.

4.4 | Types of epileptic seizures

Currently, different antiepileptic drugs are in use according to the type of seizure, and therefore, understanding the types of seizures is considered essential. The results of previous studies have revealed that generalized seizures are more

commonly seen in China,^{19,20,29} whereas focal seizures are more popular in developed countries.³⁰ Generalized epilepsy is more commonly observed in our study sample (accounting for 68.63% cases), which might be caused by the absence of electroencephalogram and neuroimaging, insufficient examiner experience and incorrect perception about epilepsy among the studied population, resulting in misdiagnosis of focal seizures. Focal seizures secondary to generalized seizures are misclassified as generalized seizures.

4.5 | Active epilepsy and treatment gaps

Several studies carried out in different countries and regions showed a significant gap in epilepsy treatment. The treatment gap in developed countries is usually lower than that of developing countries.³¹ This gap was 62.6% in five provinces of China¹⁹ and 58.97% in rural areas of Hainan Province, but showed no significant differences. These results revealed that the residents in rural areas of this province have limited awareness concerning epilepsy and there were no standardized treatment guidelines. Therefore, it is necessary to strengthen standard medical treatment strategies in rural areas and increase the awareness of epilepsy in individuals.^{30,32}

4.6 | Comparison of Hainan region with other tropical regions

Similar to other tropical regions, the climate of Hainan Province is mild, with alternating wet and dry seasons and there is no cold season. The prevalence of epilepsy in this province (3.06‰) was significantly lower than that in other tropical areas, including sub-Saharan Africa (1.5%), Latin America (1.78%), and India (0.5%-1.0%).^{10,17} Due to aging population, the leading cause of death and the most common cause of epilepsy in China remained stroke, while the primary cause of epilepsy in India and Latin America/Africa is malaria and neurocysticercosis, respectively. Cysticercosis is a parasitic infection caused by larval cysts of the pork tapeworm *taenia solium* and a combined prevalence of active and inactive epilepsy accounted to 29 per 1000 persons, causing neurocysticercosis.^{12,33} Other causes include viral encephalitis, HIV infection, craniocerebral trauma, and genetic factors, and these indicate that the causes of epilepsy varies across different tropical regions. Cerebral malaria (CM) is especially suspected to be a potential cause of epilepsy in the tropical regions. Recently, with eradication of malaria, there are fewer cases and less transmission in the island. Due to migration of infected African individuals, neurocysticercosis has also become a significant health problem in the developed countries. So, we speculated that the lower prevalence of epilepsy in Hainan Province might be due to better health conditions,

elimination of malaria and decreased prevalence of neuroparasitic infections as compared to Africa.^{12,33-35} However, more research should be conducted to understand the causes behind this condition and evaluate the differences in prevalence between these regions to elucidate relevant pathophysiological mechanisms and therefore can improve the prevention.

4.7 | Limitation of this study and future study directions

On the one hand, due to the consideration of funds and equipment in designing the survey, the diagnosis of epilepsy mainly relied on experienced clinical neurologists rather than EEG or magnetic resonance imaging. On the other hand, the residents' lacked knowledge about epilepsy, raising the possibility of misclassification regarding the seizure types, such as focal seizures followed by generalized seizures, as these might be wrongly classified into generalized seizures. Since the sample size in this study was relatively small, further studies with larger sample size are warranted to reduce the bias. In addition, the quality of life in epilepsy patients, social and psychological problems in individuals of tropical rural regions should also be considered.

5 | CONCLUSION

This survey revealed the understanding of demographic and epidemiological features of individuals present in the rural regions of Hainan Province. This large treatment gap provides evidence for the urgent need to improve public health and health education by taking vigorous measures. Moreover, additional studies on traditional Li medicine are necessary, and its effectiveness has overpassed the treatment gap in this province.

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CONFLICT OF INTEREST

The authors declare that there are no conflicts of interest associated with this study. We confirm that this manuscript complies with the Journal's guidelines on publication ethics.

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