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Prevalence of psychiatric disorders in Thai patients with epilepsy

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ABSTRACT

Background: Many studies have shown that the prevalence of psychiatric disorders in patients with epilepsy (PWE) appears higher than that in general population. However, most epidemiological studies regarding psychiatric comorbidities among PWE were conducted in Western countries. This work aimed to determine the prevalence of psychiatric disorders in Thai PWE, including potential variables that could be associated with psychiatric disorders.

Methods: A cross-sectional study was conducted at Ramathibodi Hospital. A total of 170 patients (aged 18 years or older) diagnosed as having epilepsy by a neurologist were recruited at the outpatient neurology clinic. Demographic and clinical characteristics were collected. Participants were evaluated for any psychiatric disorders according to the *Diagnostic and Statistical Manual of Mental Disorders*, 4th edition, using a structured diagnostic interview. The prevalence of psychiatric disorders was determined. The associations between potential variables and the presence of psychiatric disorders in PWE were analyzed using chi-square or Fisher's exact tests, *t*-test, and logistic regression.

Results: Among 170 patients, 43 (25.3%) fulfilled diagnostic criteria for one or more psychiatric disorders. The prevalence of depressive disorders was shown to be highest at 17.1%, followed by psychotic disorders (8.2%), bipolar disorder (7.1%), anxiety disorders (5.3%), and obsessive–compulsive disorder (OCD) (2.9%). Electroencephalogram (EEG) abnormalities in the temporal lobe was found to be a significant predictor of having psychiatric disorders in PWE (adjusted odds ratio (OR): 4.01, 95% confidence interval (CI): 1.47–10.92, P-value = 0.007).

Conclusions: The prevalence of psychiatric disorders among Thai PWE was higher than that in general population. Screening for psychiatric disorders in PWE is recommended, especially among those who have EEG abnormalities in the temporal lobe.

1. Introduction

Psychiatric disturbances have been recognized as common comorbidities in patients with epilepsy (PWE), leading to poor quality of life and increased mortality [1–3]. A recent study evaluated psychosocial characteristics and quality of life in 404 individuals with drug-resistant epilepsy. The results found that anxiety, depression, felt sigma, and low perceived self-mastery were associated with low quality of life among these patients [2]. Another case–control study on the association between epilepsy and suicide conducted in Denmark, identified 21,169 cases of suicide and 423,128 controls and found that people with epilepsy had three times higher chance of suicide compared with those without [3]. Also, psychiatric illnesses in PWE contributed to higher rates of health service utilization [4,5]. A study in the UK using data from the national morbidity survey reported that PWE consulted for mental health disorders more than twice as often as people without epilepsy and required almost fourfold more home visits [4]. Furthermore, psychiatric comorbidities were reported to be associated with lack of response to pharmacological treatment in epilepsy [6].

According to many epidemiologic studies, the prevalence of psychiatric disorders in PWE consistently appears higher than that in general population or healthy control groups [1,7–11]. A large sample study in 36,456 Canadians reported that the prevalence of any mental disorder was 35.5%. Among these, mood disorders were found to be the most prevalent (24.4%), followed by anxiety disorders (22.8%) [10]. In addition, another population-based cohort study revealed that people with epilepsy were at increased risk of schizophrenia and schizophrenia-like psychosis, and a family history of epilepsy was a significant risk factor for such mental illnesses [12]. Altogether, these data suggest that co-occurrence of epilepsy and psychiatric disorders is common.

To elucidate the relationship between epilepsy and psychiatric disorders, Hesdorffer and colleagues [13] conducted a longitudinal cohort

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study in the UK and found that the incidence of psychiatric disorders significantly increases both before and after the diagnosis of epilepsy. This finding suggests that there is a bidirectional relation between the two conditions. Several biological and psychological factors have been proposed to mediate the link [14–17]. For example, temporal lobe epilepsy (TLE), because of its pathology in the limbic system, has been found to confer greater risk of developing psychiatric disturbances when compared with other types of epilepsy. Nevertheless, conflicting results were also reported [1,8,9]. In addition, clinical characteristics of PWE that are prone to develop psychiatric disorders were also needed to be specified in order to search for high-risk population and provide appropriate care. However, previous reports on risk factors associated with psychiatric conditions in PWE still remain a controversy [14].

The prevalence of psychiatric disorders in PWE was reported to vary from 19 to 80% [1,7–11,17]. This wide variation might be a result of heterogeneous research methods across studies. For instance, some applied self-report questionnaires could over- or underestimate the prevalence of psychiatric disorders because of response bias. Using nondiagnostic assessment instruments could similarly overidentify the cases as they only detect psychiatric symptoms but do not determine definite clinical diagnoses. Moreover, most epidemiological studies to date regarding psychiatric disorders among PWE were conducted in Western countries. Since sociocultural context is also a significant contributing factor of psychiatric conditions, previous reports might not perfectly reflect the magnitude of this problem in Asian populations. In Thailand, there are few studies regarding mental comorbidities in PWE [18,19]. These studies focused only on depression and anxiety and did not apply standardized psychiatric interview for certain diagnoses. Additionally, factors associated with psychiatric disturbances in PWE were not well explored. Therefore, the present study aimed to determine more accurate prevalence of psychiatric disorders among Thai PWE using a structured diagnostic interview and to explore potential variables that could be associated with psychiatric disorders.

2. Material and methods

This work was a cross-sectional study carried out at the outpatient neurology clinic at Ramathibodi Hospital (a university hospital in Bangkok, Thailand). The clinic provides care for a broad range of neurological conditions, including epilepsy. All patients aged 18 years or older and diagnosed as having epilepsy by a neurologist were recruited between October 2016 and August 2017. The diagnosis of epilepsy was made in accordance with the International League Against Epilepsy [20]. We excluded those with serious medical conditions, mental retardation, major neurocognitive disorder, inability to speak, or severe hearing impairment. Patients who rejected to participate in the project were also excluded. This current study is part of a research project called "Psychiatric Conditions in Patients with Epilepsy in Ramathibodi Hospital". The project was approved by the Ethics Committee on Human Experimentation of the Faculty of Medicine, Ramathibodi Hospital, Mahidol University, Bangkok, Thailand (ID 07-59-08).

2.1. Measures

2.1.1. Mini-International Neuropsychiatric Interview (M.I.N.I)

The M.I.N.I [21] was developed as a brief structured diagnostic interview for psychiatric disorders according to international criteria, including the *Diagnostic and Statistical Manual of Mental Disorders*, 4th edition (DSM-IV) and the 10th revision of the International Statistical Classification of Diseases and Related Health Problems (ICD-10). It was designed to allow administration by nonspecialized interviewers. The M.I.N.I. has been widely translated, and a Thai version is also available. The M.I.N.I. Thai version 5.0.0 demonstrated excellent specificities (>90%) for the diagnosis of all psychiatric disorders [22]. Fleiss' kappa values for the interrater reliability tests range from 0.40 to 1.00 (mean = 0.89).

2.2. Procedure

Written informed consent was obtained from all participants after they had received complete information about the study protocol. Demographic data and clinical characteristics were collected from a direct interview and medical records. The M.I.N.I. Thai version 5.0.0 was then administered for the diagnosis of psychiatric disorders through a face-to-face interview. Participants' electroencephalogram (EEG) reports were also collected. In this study, abnormal EEG findings included epileptiform discharges and/or slow activity in specific brain regions.

2.3. Statistical analyses

Data analyses were conducted using Predictive Analytics SoftWare (PASW) Statistics for Windows, Version 18.0.0 (SPSS Inc., Chicago, IL, USA). Demographic and clinical characteristics of participants with psychiatric disorders and of those without psychiatric disorders were compared using *t*-test for continuous data and chi-square or Fisher's exact tests for categorical data. For categorical variables with multiple levels that show significant difference in their distributions between the two groups of patients, post-hoc analysis was then performed. P-value <0.05 was considered statistically significant. Logistic regression was used to investigate the relationship between potential predictors and the presence of psychiatric disorders in PWE.

3. Results

3.1. Demographic characteristics

A total of 170 PWE were enrolled in this study. The mean age of participants was 43.5 years (SD = 15.8). Most participants were female and single. Almost one-half (46.5%) had low income, and just over one-third (36.5%) were not currently employed. Demographic characteristics of the study sample are demonstrated in Table 1. The results showed no significant association between demographic characteristics and the presence of psychiatric disorders among PWE.

Table 1
Demographic characteristics and their associations with psychiatric disorders.

	Psychiatric disorders	Psychiatric disorders	P-value
	Present (N = 43)	Absent (N = 127)	
Age in years, mean (SD)	42.9 (15.4)	43.7 (16.0)	0.976
Female, N (%)	28 (65.1)	72 (56.7)	0.332
Marital status, N (%)			0.444
Single	25 (58.1)	72 (56.7)	
Married	13 (30.2)	47 (37.0)	
Divorce or widowed	5 (11.6)	8 (6.3)	
Education level, N (%)			0.449
Primary school or lower	12 (27.9)	24 (18.9)	
Secondary school or high school	11 (25.6)	34 (26.8)	
Diploma	2 (4.7)	14 (11.0)	
Bachelor degree or higher	18 (41.9)	55 (43.3)	
Occupation, N (%)			0.088
Unemployed	17 (39.5)	45 (35.4)	
Employed	19 (44.2)	72 (56.7)	
Student	4 (9.3)	2 (1.6)	
Retired	3 (7.0)	8 (6.3)	
Salary in baht per month, N (%)			0.560
0–9000	22 (51.2)	57 (44.9)	
9000–15,000	3 (7.0)	19 (15.0)	
15,000–30,000	11 (25.6)	34 (26.8)	
>30,000	7 (16.3)	17 (13.4)	
Comorbid medical illnesses, N (%)			0.238
Absent	22 (51.2)	78 (61.4)	
Present	21 (48.8)	49 (38.6)	

3.2. Prevalence of psychiatric disorders in PWE

Overall, 43 (25.3%) of 170 PWE fulfilled diagnostic criteria for at least one psychiatric disorder (Fig. 1). The most common psychiatric disorders in this study sample appeared to be depressive disorders with the prevalence of 10% (ten patients had major depressive disorder, five had dysthymia, and two had both conditions). The prevalence of other major psychiatric disorders was shown in the following: psychotic disorders (8.2%), bipolar disorder (7.1%), anxiety disorders (5.3%), and obsessive–compulsive disorder (OCD) (2.9%). Eleven (6.5%) patients met the criteria for two or more mental disorders. None of the PWE met the criteria for substance use disorders, eating disorders (anorexia nervosa and bulimia nervosa), or antisocial personality disorder.

3.3. Clinical characteristics

Table 2 illustrates the clinical characteristics of the participants. Seventy-eight (45.9%) were diagnosed with epilepsy by the age of 16 years. Around a quarter reported that they had seizures once a month or more. Almost 90% were taking at least one type of antiepileptic medications. None of these factors (age at epilepsy onset, frequency of seizure, and number of antiepileptic drugs) demonstrated significant associations with the presence of psychiatric disorders.

Electroencephalogram reports were available in medical records of only 95 participants. Seventy (73.7%) patients had abnormal waveforms in one or more brain regions; 34 in temporal, 14 in frontal, 13 in frontotemporal, and nine in other regions. A significant association between EEG abnormalities and the presence of psychiatric disorders was observed (χ^2 (4, N = 95) = 10.99, P = 0.027). Post-hoc analysis revealed that the odds of psychiatric disorders among patients with abnormal EEG findings in the temporal area was 3.28 times (odds ratio (OR): 3.28, 95% confidence interval (CI): 1.36–7.89) the odds among those with normal or abnormal EEG findings in other brain areas. Neither the absence of EEG abnormalities nor their presence in other brain regions was associated with psychiatric disorders (Table 2). After adjusting for potential confounding factors, including age, sex, education level, comorbidity of medical illnesses, and age at epilepsy onset, the presence of EEG abnormalities in the temporal region still remained a significant predictor of having psychiatric disorders among PWE (adjusted OR: 4.01, 95%CI: 1.47–10.92, P-value = 0.007).

Table 2
Clinical characteristics and their associations with psychiatric disorders.

	Psychiatric disorders	Psychiatric disorders	P-value
	Present (N = 43)	Absent (N = 127)	
Age at epilepsy onset (years), N (%)			0.817
0–15	18 (41.9)	60 (47.2)	
16–30	10 (23.3)	29 (22.8)	
31–60	12 (27.9)	27 (21.3)	
>60	3 (7.0)	11 (8.7)	
Frequency of seizure, N (%)			0.997
3 or more times per week	3 (7.0)	9 (7.1)	
1–4 times per month	8 (18.6)	23 (18.1)	
Once per year or less	32 (74.4)	95 (74.8)	
EEG abnormality in specific brain region, N (%)[a]			0.027
Frontal lobe	2 (5.6)	12 (20.3)	0.049
Temporal lobe	19 (52.8)	15 (25.4)	0.007
Frontotemporal lobe	2 (5.6)	11 (18.6)	0.122
Others	4 (11.1)	5 (8.5)	0.726
Not detected	9 (25.0)	16 (27.1)	0.820
Number of antiepileptic drugs, N (%)			0.276
0	6 (14.0)	12 (9.4)	
1	20 (46.5)	67 (52.8)	
2	15 (34.9)	32 (25.2)	
3 or more	2 (4.7)	16 (12.6)	

[a] Unavailable data not included for calculation.

4. Discussion

The relationship between epilepsy and mental disorders has been noted in a number of studies in Western countries [15–17]. However, the findings might not be applied to Asian population because of the difference in sociocultural context, which is a significant contributing factor of the development of psychiatric disorders. In this study, we found that 25.3% of PWE had at least one psychiatric disorder, almost twice as much as the prevalence in general Thai population [23,24]. Our data corroborate with those from large population-based studies in Canada [10] and the UK [25]. Tellez-Zenteno et al. reported that the prevalence of mental disorders among PWE was 23.5%, compared with 10.9% in Canadian general population [10]. Similarly, in the UK, the prevalence ratio of psychiatric disorders in PWE was doubled in both young and older adults compared with the population without epilepsy [25]. Such consistently high rates of psychiatric disorders among PWE across a variety of sociocultural contexts underscore a significant connection between the two conditions and also, highlight the clinical importance of psychiatric comorbidities among these particular groups of patients.

In our sample, 17.1% of the patients met the diagnostic criteria of mood disorders, which appeared to be the most prevalent psychiatric disturbances among Thai PWE. The rate of affective disturbances in our study was comparable with that reported in previous studies using structured diagnostic interview [9,10,25]. However, the prevalence appears higher, ranging from 36 to 55%, when nondiagnostic self-reported or symptom-rating scales were used [8,19,26,27]. This variation could result from difference in evaluation methods across studies — in other words, a validated interview needs more stringent criteria in diagnosis of the conditions, contributing to lower rates of cases being identified. Similarly, while our study, using a diagnostic interview, observed the prevalence of anxiety disorders at 5.3%, approximately three times that in general population [23,24], a previous study in Thai patients with epilepsy that used a self-rated screening instrument reported a much higher rate of anxiety symptom at almost 40% among PWE [18]. A structured clinical interview is considered as a standard method in making psychiatric diagnosis; however, it could overlook atypical manifestations and subclinical symptoms of emotional disturbances that are severe enough to call for clinical attention [28,29]. Indeed, a specific emotional disorder namely an interictal dysphoric disorder has been proposed among PWE [28,29]. Patients with this condition tend to have somatic symptoms and mood disturbances that do not meet the DSM criteria for mood disorders but may require pharmacological management. Hence, the actual size of clinically significant affective problems among Thai PWE could be larger than what we found in the present study.

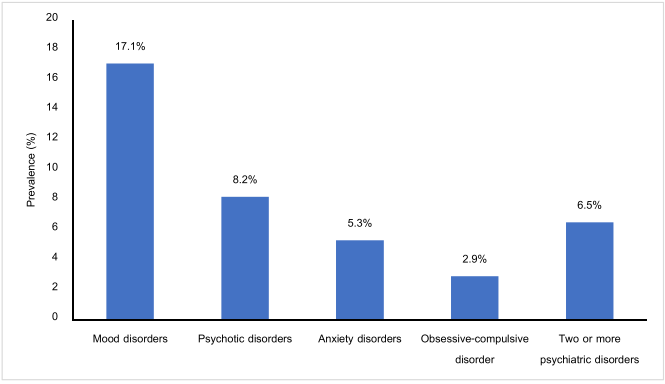

Fig. 1. Prevalence of psychiatric disorders in patients with epilepsy.

Psychotic disorders are severe psychiatric conditions that markedly disrupt a person's thinking and behaviors but were not well explored in Thai PWE. In our study, psychotic disorders were detected in 8.2% of the PWE, over 16 times of that derived from a Thai adult survey [23]. This finding was consistent with the data from a recent meta-analysis showing that the pooled estimated prevalence of psychosis in PWE was 5.6%, and the pooled odds ratio for the condition was 7.8 compared with control groups [30]. Another cohort study of 2.27 million people also found that those with a history of epilepsy have almost 2.5 times the risk of developing schizophrenia compared with those without [12]. The increased risk might be partly explained by the effect of seizure on psychosis-related brain regions, including hippocampal, amygdala, and septal area, or shared cerebral dysfunction that might lead to co-occurring of both epilepsy and psychosis [17,31,32].

Interestingly, eating disorders and antisocial personality disorder were not detected in our study population. This might be partly explained by low prevalence of these disorders in general as well as limited condition assessed by the M.I.N.I. Indeed, a study in Australian general population revealed that the prevalence of anorexia nervosa and bulimia nervosa was less than 1% whereas those of binge eating disorder and subthreshold binge eating disorder were 5.6–6.9% [33]. Another two studies using self-report nondiagnostic questionnaires also illustrated that around 5% of PWE had eating disorder symptoms [11, 34]. Since the M.I.N.I was designed to detect merely anorexia nervosa and bulimia nervosa, but not other eating disorders, these evidence could imply that the former two disorders are much less common in PWE than binge eating disorder as well as subthreshold eating disorder symptoms. Similarly, antisocial personality disorder was found to be far less prevalent in PWE than avoidant and dependent personality disorders, which were the two most common personality disorders among this population but were not included in the M.I.N.I. [35,36].

We did not find PWE who meet the diagnostic criteria for substance use disorder in this study. In contrast, some reports showed that the condition was not uncommon, especially among male patients [25,37]. As about two-thirds of the subjects in the present study were women, we hypothesized that the female preponderance might, at least partly, explain such surprisingly low prevalence of the disorder. Furthermore, report bias could potentially be another issue particularly for socially undesirable behaviors including substance use, rendering false negative results.

Apart from prevalence estimation, we also intended to identify factors plausibly associated with psychiatric disorders in this population. The logistic regression revealed that patients with EEG abnormalities in the temporal region had four times greater risk of having psychiatric disorders compared with those with normal EEG or EEG abnormalities in other brain regions. The results were supported by several articles, which indicated that patients with TLE are at an increased risk of psychiatric comorbidities [8,17,32,38]. However, a study in 209 patients in a tertiary epilepsy center found no significant differences between TLE and extra-TLE on the prevalence of psychiatric disorders [9]. Though the controversy went on, future research determining how TLE affects the existence of mental disturbances compared with non-TLE may shed some light on this issue.

The present study also had some limitations. First, we conducted this study in a university hospital; thus, our population might not be a representative of PWE in other settings. Second, people without epilepsy were not included as a control group in our study. Instead, the prevalence ratios of psychiatric disorders derived from two recent, large Thai national population studies were used for comparison. Next, EEG data were not available in almost half of the patients; thus, the sample size is reduced for the related analyses. Last, the cross-sectional design of our study does not allow for causal inferences. Thus, longitudinal studies are required to clarify the causal pathways of our observation.

The obvious strength of our study is the evaluation method for mental disorders. We administered a structured psychiatric interview that has been well validated and widely used as a clinical diagnostic tool for Thai people. Hence, the prevalence of major psychiatric disorders reported in this study should reflect more accurate estimation of the size of psychiatric problems. Additionally, our findings were supposed to raise the alertness of healthcare professionals taking care of PWE to recognize these prevalent comorbidities, especially in those at high risk. We also proposed that routine screening and appropriate referral to mental health services should be included as standard care to improve quality of life in PWE.

5. Conclusions

The prevalence of psychiatric disorders among PWE was higher than that in general population. Clinicians and healthcare professionals taking care of PWE should be aware of an increased risk of developing psychiatric comorbidities and also, alert to look for the conditions among this particular population. Systemic approaches are needed to improve the quality of mental healthcare for PWE. Screening instrument may be helpful for early detection of psychiatric disorders, especially among patients who have EEG abnormalities in the temporal lobe.

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Author disclosures

The authors declare no competing interests.

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