

## Depression in people with epilepsy: How much do Asian colleagues acknowledge it?

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### ABSTRACT

**Purpose:** The purpose of this review was to investigate the prevalence of depression in people with epilepsy (PWE) in different countries in Asia.

**Methods:** We searched the electronic database PubMed on June 13, 2017 for articles in English that included the following search terms: “epilepsy” AND “depression” AND “country name” for all Asian countries since 1947. Relevant original studies from Asia were included if they reported the prevalence of depression in PWE. Papers studying special populations (e.g., elderly, veterans, etc.) were not included. In addition, experts in epilepsy field were invited from some Asian countries for an in-depth assessment. **Results:** Six hundred eighty-seven papers were reviewed and 26 related studies were included in this study. Depression is highly prevalent in PWE in different countries in Asia and the prevalence rates are consistent with rates reported in the literature from other countries: overall, about 25% of PWE suffer from depression.

**Conclusion:** In Asian countries, as elsewhere, depression is common in PWE. High quality data is scarce in many countries and validated screening tools [e.g., Neurological Disorders Depression Inventory for Epilepsy (NDDI-E)] to appropriately investigate the prevalence of depression in PWE are still lacking in many languages. Considering the high prevalence of depression among PWE, routine and periodic screening of all PWE for early detection and appropriate management of depression would be a reasonable approach.

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### 1. Introduction

Depression has been observed to be highly prevalent in people with epilepsy (PWE). A systematic review and meta-analysis of its prevalence, revealed a 23.1% (95% confidence interval [CI] 20.6%–28.31%) [1] prevalence of active depression which is much higher than that in the general population. In a population-based study [2], the average lifetime and 12-month prevalence estimates of major depressive episodes were 14.6% and 5.5%, respectively in the 10 highest-income countries, and 11.1% and 5.9% in the eight

countries with low- to middle-income. However, depression is often under-recognized and improperly treated in PWE, which is associated with work absenteeism, increased utilization of health care services and direct medical costs [3,4]. Asia is the most populated continent in the world and is very diverse with respect to culture, ethnicity, religion, and other socio-demographic characteristics of the residents compared with the people in other continents. Studies about epilepsy and its comorbidities, including depression, are lacking from many Asian countries. The purpose of this review was to investigate the prevalence of depression in PWE in different countries in Asia. We also investigated how depression and depressive symptoms were evaluated in different studies in distinct Asian countries.

## 2. Methods

We searched the electronic database PubMed on June 13, 2017 for articles in English that included the following search terms: “epilepsy” AND “depression” AND “country name” for all Asian countries since 1947. If the initial search resulted in a high number of papers (>40 papers), we limited the search to the title and abstract for all countries and searches. Relevant original studies from Asia were included if they reported the prevalence of depression in PWE. Papers studying special populations (e.g., elderly, veterans, etc.) were not included.

In addition, experts in epilepsy field were invited from some Asian countries (Japan, China, Korea, Thailand, Taiwan, and Iran). Each expert was asked to review the prevalence of depression in their country based on the previously published literature for an in-depth assessment.

## 3. Results

Six hundred eighty-seven papers were reviewed and 26 related studies were included in this study. Table 1 shows the number of published papers, the prevalence of depression and the scales applied by researchers to screen for depression in these patients in each Asian country.

The following paragraphs are the results of the expert review of the prevalence of depression in PWE in some Asian countries for an in-depth assessment. It was desirable to have consistent description of the findings related to each country. But, such results were not available consistently. That is why studies of risk factors for depression, suicidality and other variables are included in some countries, but not in others.

### *Depression in PWE in Japan*

Prevalence of major depression (2.9%) was reported to be lower in Japan compared to that in the Western countries [2,5]. The Japanese version of the Neurological Disorders Depression Inventory for Epilepsy (NDDI-E) was developed in 2012 [6]. The prevalence of depression in PWE was 18.6% in one study [7], which is very similar to the reports from other countries [1]. In another study [8], authors compared the symptoms of depression in PWE and those with primary depression, using three screening instruments: the Beck Depression Inventory II (BDI-II) [Ref], the Center for Epidemiologic Studies Depression Scale (CES-D) [Ref] and the Buss-Perry Aggression Questionnaire (BAQ) [Ref]. They observed that the anger item was significantly more frequent in PWE [8].

### *Depression in PWE in South Korea*

Depression is the 3rd most common psychiatric disorder in Korea; however, the life-time prevalence of major depressive disorder (MDD) in Korea (3.3%–5.6%) was reported to be lower

compared with that in the Western countries [2,9]. In Korean PWE, the prevalence of MDD was reported to be ranged from 21.5% to 27.8% [10–12]; a very similar finding to that of the reports from other countries [1]. In a Korean multicenter study, PWE with MDD were 15.6 times at higher risk of developing suicidality than PWE and without MDD [10]. Major risk factors for suicidality were MDD, generalized anxiety disorder, and adverse effects of antiepileptic drugs. Odds ratio of suicidality increased up to 45.5 compared with that in patients with no risk factors, when the three risk factors were conjoined. Despite the fact that MDD was a main risk factor of suicidality, a majority of these patients had never undergone psychiatric interventions [10]. That means depression in Korean PWE remains significantly under-recognized and under-treated.

The Korean version of the Neurological Disorders Depression Inventory for Epilepsy (K-NDDI-E) has been developed and validated [12]. A cutoff score suggestive of MDD in K-NDDI-E is 11, which is much lower than that of the original version [12].

### *Depression in PWE in China*

The lifetime prevalence of MDD in China (3.6%) has been reported as being lower than that in Western countries [2,13]. Studies from different regions of China have used different scales and revealed that 16.5% to 43.4% of Chinese PWE have comorbid depression [14–20]. Studies that investigated the risk factors associated with depression in Chinese PWE [15,16] identified: drug resistance, a history of chronic medical illnesses, unemployment, age >35 years, female gender, having focal epilepsy, history of status epilepticus, and using topiramate. In 2015, the Neurological Disorders Depression Inventory for Epilepsy (NDDI-E) was translated and validated into a Chinese version (C-NDDI-E) in Western China. The authors found that the C-NDDI-E was a reliable screening tool, with a cut-off score >12 suggestive of a major depressive episode [17]. They found a prevalence of possible MDE of 26.7%. In another study conducted in East China, the authors found a higher cut-off score (>13) for the C-NDDI-E [14].

### *Depression in PWE in Thailand*

Using the Thai Geriatric Depressive Scale (TGDS), one hospital-based study [21] suggested a prevalence of depression in PWE in Thailand to be 38.3%; 65.2% had mild depression and 34.8% had moderate depression. Using the Hospital Anxiety and Depression Scale (HADS) a hospital-based study [22] suggested a 20% prevalence rate.

### *Depression in PWE in Taiwan*














































A comparison of prevalence rates of psychiatric disorders in Taiwanese adults 1990 and 2010, revealed an increment from 11.5% in 1990 to 23.8% in 2010 (time trend  $p < 0.001$ ) [23]. A population based study using the national health insurance research database showed that patients with a new diagnosis of epilepsy had higher occurrence of depression than those without epilepsy (adjusted hazard ratio: 7.16, 95% CI 4.87–10.5) [24]. In another population based study using the national health insurance research database [25], psychiatric comorbidities were present in 24.6% of children with epilepsy. However, no PWE was diagnosed with MDD [25]. Using the HADS in one clinic based study of 260 PWE [26], 8.5% had scores suggestive of moderate to severe depression and 14.2% of mild depression.

### *Depression in PWE in Iran*

In a population based study that used a validated Persian translation of the Composite International Diagnostic Interview

**Table 1**

Number of published papers, the prevalence of depression in people with epilepsy (PWE), and the scales applied by researchers to identify depression in these patients in each Asian country.

Country	Initial Papers with the Keywords of Depression and Epilepsy	Relevant Papers on Depression in Epilepsy	Range of Depression in PWE	Scale used: % depression in PWE
 Afghanistan	1	0	–	–
 Armenia	1	0	–	–
 Azerbaijan	0	0	–	–
 Bahrain	1	0	–	–
 Bangladesh	2	1	20%	DAWBA [36]
 Bhutan	0	0	–	–
 Brunei	0	0	–	–
 Cambodia	0	0	–	–
 China	126	7	16.5%–43.4%	C-MINI: 16.5% [14] BDI: 19.6% [18] HAMD: 19.8% [16] C-NDDI-E: 26.7% [17] DSM-IV-TR criteria for major depression: 30.2% [15] HADS: 33.2%–43.4% [19,20] Patient Health Questionnaire –09 (based on DSM-IV criteria) [37]
 India	126	1	23.8%	–
 Indonesia	1	0	–	–
 Iran	43	2	10.7%–35%	SADS: 10.7% [28]
 Iraq	2	0	–	BDI: 35% [29]
 Israel	51	0	–	–
 Japan	143	1	18.6%	J-NDDI-E [7]
 Jordan	9	2	22.8%–42%	DSM-IV criteria: 22.8% [38] NPI: 42% [39]
 Kazakhstan	1	0	–	–
 Kuwait	1	0	–	–
 Kyrgyzstan	0	0	–	–
 Laos	0	0	–	–
 Lebanon	25	0	–	–
 Malaysia	8	1	12%	HADS [40]
 Maldives	1	0	–	–
 Mongolia	0	0	–	–
 Myanmar	0	0	–	–
 Nepal	1	0	–	–
 North Korea	0	0	–	–
 Oman	2	1	27%	HADS [41]
 Pakistan	10	1	60%	Semi structured interview based on ICD-10 [42]
 Philippines	0	0	–	–
 Qatar	1	0	–	–
 Saudi Arabia	10	1	6.6%	HADS [43]
 Singapore	9	0	–	–
 South Korea	51	3	21.5%–27.8%	K-MINI: 21.9% [10] BDI: 27.8% [11] K-NDDI-E: 21.5% [12]
 Sri Lanka	0	0	–	–
 Syria	1	0	–	–
 Taiwan	42	1	8.5%	HADS [26]
 Tajikistan	0	0	–	–
 Thailand	10	2	20%–38.3%	HADS: 20% [22] TGDS: 38.3% [21]
 Timor-Leste	0	0	–	–
 Turkmenistan	0	0	–	–
 United Arab Emirates	6	2	26.9%–28.7%	Patient Health Questionnaire nine-item depression scale (PHQ-9) [44,45]
 Uzbekistan	0	0	–	–
 Vietnam	1	0	–	–
 Yemen	1	0	–	–

PWE: people with epilepsy; DAWBA: Development And Well-Being Assessment; HADS: Hospital Anxiety and Depression Scale; BDI: Beck Depression Inventory; C-NDDI-E: Chinese version of the Neurological Disorders Depression Inventory for Epilepsy; HAMD: Hamilton Depression Rating Scale; C-MINI: The Chinese version of the Mini International Neuropsychiatric Interview; SADS: Schedule for Affective Disorders and Schizophrenia; J-NDDI-E: Japanese version of the Neurological Disorders Depression Inventory for Epilepsy; K-MINI: Korean version of the Mini International Neuropsychiatric Interview; K-NDDI-E: Korean version of the Neurological Disorders Depression Inventory for Epilepsy, TGDS: Thai Geriatric Depressive Scale; NPI: Neuropsychiatric Inventory.

(CIDI; version 2.1) [27], the 12-month prevalence of MDD was 12.7%, which was higher than that in many other countries [2]. In one cross-sectional nationwide epidemiological study of the Iranian population using the Schedule for Affective Disorders and Schizophrenia (SADS) [28], 10.7% of the PWE had major depression and 1.3% had minor depression; these figures were 3% and 0.3% in the general population, respectively [28]. In one cross-sectional hospital based study of 74 adult PWE [29], 26 (35%) patients had symptoms of depression identified with the Beck Depression Inventory (BDI). In one clinic based study of children in Iran [30], the mean scores of the Child Symptom Inventory-4 (CSI-4) were significantly higher among children with epilepsy compared with those of a control group (major depression score:  $10.5 \pm 3.8$  in the epilepsy group and  $7.7 \pm 1.1$  in the control group,  $P < 0.001$ ) [30].

#### 4. Conclusions

Depression is highly prevalent in PWE in different countries in Asia and the prevalence rates are consistent with rates reported in the literature from other countries: overall, about 25% of PWE suffer from depression [31]. Interestingly, the apparent cultural, demographic, religious, and ethnic diversity in Asia has not affected the prevalence of this comorbidity significantly. This is notably the case even in countries such as China and Japan, where depression rates in the general population are lower than those in many Western nations [2,5,7,13,14]. Cultural differences in the expression of depression are important and well-recognized. While depression is a universal experience, its acceptance is highly dependent on many social and cultural aspects that interplay with each person's emotional development over their lifetime [32,33]. For example, in some cultures open expression of grief or suffering is encouraged, while in other cultures such emotions should be concealed. The latter may lead to under-estimation of the depression rate in population and hospital-based investigations. In addition, the role of clinical care may be viewed very differently depending up on the cultural context: for some cultural backgrounds, depression may be considered more of a moral or spiritual problem than a medical one, which may result in reluctance to consulting a physician, reporting symptoms or following medical advice [32]. Despite the growing effects of globalization, such cultural differences seem likely to persist, or even be reinforced by a desire to protect ethnic identity, and should be taken into account when studying depression across international boundaries [34].

In Asian countries, as elsewhere, depression is often under-recognized and improperly managed in PWE [10]. High quality data is scarce in many countries and validated screening tools [e.g., Neurological Disorders Depression Inventory for Epilepsy (NDDI-E)] to appropriately investigate the prevalence of depression in PWE are still lacking in many languages. This study was not a meta-analysis or a classical systematic review. It is possible that some manuscripts that could be relevant for this review were excluded without review. In spite of this limitation, this study provides the foundation for future systematic research in the field. In addition, since, different studies used various tools to investigate the prevalence of depression and depressive symptoms and also because the settings of the investigations were very variable, an analysis on the overall results was not scientifically valid in the current study. Questionnaires and scales, such as NDDI or BECK, address depressive symptoms, not a depressive disorder. Depression is a psychiatric diagnosis evaluated by a psychiatric interview. This distinction was not clear in most of the literature. A systematic review of the validated tools for depression screening in PWE concluded that NDDI-E was the most commonly validated screening tool, is validated in multiple languages and is easy to

administer [35]. However, varying cut-off points exist in different languages [31]. This may result in variable outcomes when studying depression in different regions [4,17]. Availability of NDDI-E in different languages will facilitate easier recognition of depression in PWE and may lead to appropriate treatment of this comorbid disorder, as well as facilitating cross-cultural studies. However, a uniform methodology (e.g., study settings and population) among different languages and cultures in validating this tool seems necessary. Considering the high prevalence of depression among PWE, routine and periodic screening of all PWE for early detection and appropriate management of depression would be a reasonable approach.

#### Conflicts of interest

Ali A. Asadi-Pooya, M.D., consultant: Cerebral Therapeutics, LLC and UCB Pharma; Honorarium: Hospital Physician Board Review Manual, Cobel Daru; Royalty: Oxford University Press (Book publication); others: no conflict of interest; Professor Kanemoto has received educational grants and speaker's fees from UCB, Otsuka Pharmaceuticals, GSK, Eisai, and Daiichi-Sankyo.

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