

Suicidal ideation amongst epilepsy patients in a tertiary centre

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Abstract

Background and Objective: Epilepsy and depression are interlinked and lead to an increased risk of suicidal ideation and suicide. Although depression is a significant risk factor for suicidal ideation in epilepsy patients, epilepsy itself is independently associated with suicidal ideation. There are various other factors related to epilepsy that further increase this risk. **Methods:** We conducted a study of suicidal-ideation amongst epilepsy patients in our centre. Demographic data and clinical history were obtained while suicidal ideation was determined using the Columbia Suicide Severity Rating Scale (C-SSRS). Beck's Depression Inventory-II (BDI-II) was used to identify presence of depression. **Results:** We recruited 80 patients with epilepsy and an equal number of controls. Epilepsy patients were more likely to be depressed with a mean BDI-II score of 9.09 ± 6.48 compared to controls who has a mean score of 5.56 ± 4.56 . The proportion of epilepsy patients with suicidal ideation was 33.75% vs. 5.00% in the control group ($p < 0.001$). Epilepsy patients were 9.68 times more likely to have suicidal ideation compared to controls: OR 9.68 (95% CI 3.19, 29.28). Amongst epilepsy patients, those with suicidal ideation were more likely to be on 3 or more anti-epileptic drugs (10.00% vs. 6.25%, $p = 0.016$), with a higher seizure frequency (11.25% vs. 2.50%, $p = 0.004$) and higher incidence of previous head surgery (10.00% vs. 5.00%, $p = 0.022$).

Conclusion: Suicidal ideation was significantly prevalent amongst epilepsy patients especially in patients with frequent seizures, use of ≥ 3 anti-epileptic drugs or prior head surgery. Our findings suggest that assessment of suicidal ideation is pertinent in high-risk epilepsy patients and should be routinely carried out in the clinical setting.

INTRODUCTION

Mood disorders are prevalent in epilepsy disorders, particularly major depression, anxiety disorder, schizophrenia and substance abuse. Depression not only affects the quality of life but is also a predictor for suicidal ideation in epilepsy patients.¹⁻⁴ Individuals with prolonged depressive disorder were likely to exhibit anhedonia and suicidal ideation. Studies on prevalence of suicide in epilepsy are reported at 5-10% whereas the prevalence of suicidal ideation was quoted as high as 36.7%.⁵

Numerous risk factors for suicide and suicidal ideation identified were early onset of epilepsy diagnosis, temporal lobe epilepsy ad complex partial seizures, and female gender. Recent data

has emerged to link anti-epileptic drugs (AEDs) to suicidal ideation or tendencies. This cumulated in the *United States Food and Drug Agency* (US-FDA) to issue an alert and warning in January 2008 linking anti-epileptic drug to that of suicidal ideation.⁶

In view of the overwhelming supporting evidences, there is a clear need to ascertain the prevalence of suicidal ideation in epilepsy patients in our local population. There are currently no available data locally or for South East Asian region as regards to the prevalence and rate of suicidal ideation in epilepsy patients. We therefore conducted this study to determine the proportions and predictors of suicidal ideation in epilepsy patients in a Malaysian tertiary teaching hospital setting.

METHODS

We conducted this study in the UKM Medical Centre (UKMMC), a tertiary teaching hospital in Kuala Lumpur, Malaysia from February to August 2013. Patients were sequentially recruited in the neurology outpatient clinic and healthy controls were recruited.

All patients (or their legal guardians) and controls provided informed consent. Inclusion criteria were individuals above the age of 14 with a recognized epilepsy syndrome diagnosed by a certified neurologist. Patients with dementia, psychosis, delirium or any other pre-existing psychiatric disorder were excluded. Data collected included socio-demographic data, epilepsy subtype, imaging findings and EEG results. Data was based on patient self-report and study of the case notes. The prevalence of depression was determined using the Beck's Depression Inventory-II (BDI-II)⁷; the most widely recognized self-administered questionnaire on depression, while presence of suicidal ideation was identified by interview using the Columbia Suicide Severity Rating Scale (C-SSRS).⁸ To reduce bias, all interviews were conducted in a designated space by a single researcher.

The revised *Beck's Depression Inventory-II* (BDI-II) consisted of a 21 questions self report inventory which is widely used and seen as a benchmark to measure severity of depression. Each answer is being scored from 0 to 3. Total score would then be sum up and indicative of the severity of depression, adapted from *Beck's Depression Inventory-II* (1996)⁷; 0–13 (Minimal), 14 –19 (Mild), 20 – 28 (Moderate), 29 – 63 (Severe).

The BDI-II is copyrighted by *Pearson Education* and is therefore not reproducible in this article. Information regarding the purchase of the BDI-II manual and scale are available at their website: <http://www.pearsonclinical.com>. We initially made ready a translated and validated BDI-I in Malay⁹; the only available BDI in Malay, but however this was subsequently not taken in consideration as all subjects opted to use the English language BDI-II.

To objectively assess the suicidal severity, the scale that was utilized is the Columbia Suicide Severity Rating Scale (C-SSRS). We have obtained the kind permission of Dr. Kelly Posner and her team from *The Center for Suicide Risk Assessment, Columbia University and New York State Psychiatric Institute*. The C-SSRS was first introduced in 2006, is now considered to be the definitive suicidal rating scale and being used

extensively across research, primary care, clinical practices and institutional settings both in the United States and internationally. The C-SSRS validity has been established in three major clinical trials with high sensitivity and specificity for suicidal ideation.⁸ It is unique in that it assesses the severity, intensity, behavior and lethality of the suicidal ideation. It utilizes a scale of 1-5 with increasing severity from “a wish to die” to “the active thought of suicide with plan and intent.” This essentially classifies the patient to either just having a thought of suicide to patients having made up a proper plan (severe) towards suicide. If a patient were noted to have a suicidal thought, the C-SSRS would then ascertain the intensity of the ideation. A validated translated Malay version of the C-SSRS is also available for use in this study. Further information regarding the C-SSRS can be obtained at <http://www.cssrs.columbia.edu>

Statistical analysis

The reported prevalence of suicide in the general population and in epilepsy patients is 1.2% and 12% respectively.¹⁰ Based on this figure and assuming a two-sided significance level of 5% and with 95% confidence interval we calculated that 80 respondents in each arm to ensure an 80% level of significance.

Numerical data were subjected to normality testing using Kolmogorov-Smirnov test at which a non-significant result, $p > 0.05$ would indicate a normally distributed data. Normally distributed data was expressed as mean standard deviation (s.d.).

For normally distributed data, the significance of difference between continuous variables was tested using Independent Student's t-test. For non-normally distributed data, Mann-Whitney U or Kruskal Wallis tests were used. Categorical variables were analysed using Chi Square test or Yates' Correction test as appropriate. Correlations were tested using Spearman Rank Correlation Coefficients (r_s). A multiple logistic regression analysis using binary logistic regression was performed to calculate the odd ratio (95% CI) of risk factors.

RESULTS

In our study, the study population was divided into two: the epilepsy group and the control group with 80 patients in each arm. The average age is 37.04 ± 15.10 for the epilepsy group and 35.59 ± 15.49 for the control group. The gender

is evenly distributed with 39 (48.75%) males and 41 (51.25%) females in each arm (Table 1). The mean Beck's Depression Inventory-II (BDI-II) score in epilepsy group (9.09 ± 6.48) was significantly higher than the control group (5.56 ± 4.56) ($p < 0.01$).

In our sub-analysis of epilepsy patients, we have also analyzed characteristics of the disease itself in both the suicidal ideation group and in those without suicidal ideation. On average, the age at diagnosis of epilepsy is 24.52 ± 18.91 years old in the suicidal ideation group and 22.75 ± 13.77 years old in the non-suicidal ideation group. In terms of duration of epilepsy, the mean average was 16.52 ± 14.43 years in the suicidal group and 12.43 ± 9.94 years in the non-suicidal ideation group. The mean age for those with suicidal ideation in the epilepsy group was 41.04 ± 17.13 years old and 35.00 ± 13.67 years old in the non-suicidal ideation subgroup. From the C-SSRS assessment, there were 27 subjects (33.75%) with suicidal ideation compared to 5% in the control group. Binary logistic analysis comparing suicidal ideation in epilepsy group and control showed

an odds ratio of 9.68 (95% CI 3.19,29.28). The socio-demographic of the epilepsy group (with and without suicidal ideation) were summarized in Table 2.

The classification of epilepsy was based in the ILAE 1989 classification¹¹. In both groups, majority of patients were having generalized convulsive epilepsy (18.75% in suicidal ideation group vs. 41.25% in non-suicidal ideation group). This was followed by complex partial seizure (12.50% vs. 16.25%) and simple partial seizures (1.25% vs. 5.00%). Generalized absence seizures were present in 1.25% in the suicidal group and 2.50% in the non-suicidal ideation group (Table 3). These differences in types of epilepsy were however statistically not significant. There were no statistical significance noted when these characteristics (neuroimaging, EEG and temporal lobe involvement) were compared to epilepsy patients without suicidal ideation.

Suicidal ideation is significantly higher in epilepsy group with previous head surgery at 10.00% and 5.00% in the control group ($p=0.022$). In the suicidal ideation epilepsy patients group,

Table 1: Sociodemographic data of study population (epilepsy group vs control)

Characteristics	Epilepsy group n = 80	Control group n = 80	p-value
Age (year)			
Mean (\pm s.d.)	37.04 (15.10)	35.59 (15.49)	0.550 ^o
Range	15.0 - 75.0	15.0 - 73.0	
Gender, n (%)			
Male	39 (48.75)	39 (48.75)	> 0.999
Female	41 (51.25)	41 (51.25)	
Ethnicity, n (%)			
Malay	47 (58.75)	52 (65.00)	0.716
Chinese	23 (28.75)	20 (25.00)	
Indian	8 (10.00)	5 (6.25)	
Others	2 (2.50)	3 (3.75)	
Religion, n (%)			
Islam	47 (58.75)	54 (67.50)	0.560
Buddhist	21 (26.25)	19 (23.75)	
Hindu	8 (10.00)	4 (5.00)	
Christian	4 (5.00)	3 (3.75)	
Education Level, n (%)			
Primary	14 (17.50)	7 (8.75)	0.432
Secondary	35 (43.75)	40 (50.00)	
Tertiary	24 (30.00)	26 (32.50)	
Postgraduate	7 (8.75)	7 (8.75)	

Table 2: Sociodemographic data of epilepsy patients with suicidal ideation and non-suicidal ideation

Characteristics	Suicidal ideation	Non-suicidal	p-value
No of subjects, n (% of total)	27 (33.75)	53 (66.25)	
Age (year)			
Mean (\pm s.d.)	41.04 (17.13)	35.00 (13.67)	0.091
Gender, n (% of total)			
Male	13 (16.25)	26 (32.50)	0.939
Female	14 (17.50)	27 (33.75)	
Ethnicity, n (% of total)			
Malay	12 (15.00)	35 (43.75)	0.163
Chinese	11 (13.75)	12 (15.00)	
Others	4 (5.00)	6 (7.50)	
Education level, n (% of total)			
Primary	7 (8.75)	7 (8.75)	0.168
Secondary	13 (16.25)	22 (27.50)	
Tertiary and above	7 (8.75)	24 (30.00)	

Table 3: Baseline characteristics of epilepsy patients with suicidal ideation and non-suicidal ideation

Characteristics	Suicidal ideation	Non-suicidal	p-value
Number of subjects, n (%)	27 (33.75)	53 (66.25)	
Age at diagnosis (year)			
Mean (\pm s.d.)	24.52 (\pm 18.91)	22.75 (\pm 13.77)	0.635
Duration of epilepsy (year)			
Mean (\pm s.d.)	16.52 (\pm 14.43)	12.43 (\pm 9.94)	0.141
Type of epilepsy, n (% of total)			
Simple partial	1 (1.25)	4 (5.00)	0.855 [†]
Complex partial	10 (12.50)	13 (16.25)	0.242
Generalised convulsive	15 (18.75)	33 (41.25)	0.562
Generalised myoclonic	0 (0.00)	0 (0.00)	-
Generalised absence	1 (1.25)	2 (2.50)	> 0.999 [‡]
Unclassified seizure	0 (0.00)	1 (1.25)	> 0.999 [‡]
Previous head surgery, n (% of total)			
Yes	8 (10.00)	4 (5.00)	0.022^{†*}
No	19 (23.75)	49 (61.25)	
Seizure frequency, n (% of total)			
Daily to Weekly	9 (11.25)	2 (2.50)	0.004[*]
Monthly	5 (6.25)	13 (16.25)	
Every six monthly	6 (7.50)	15 (18.75)	
Less than yearly	7 (8.75)	23 (28.75)	
No of AEDs, n (% of total)			
1	10 (12.50)	37 (46.25)	
2	9 (11.25)	11 (13.75)	
3 or more	8 (10.00)	5 (6.25)	0.016[‡]

p-value calculated using Pearson's Chi Square, with exception of calculated by independent *t*-test, [†] by Yates' correction. [‡] by One-Way ANOVA (Tukey Post Hoc analysis) comparing 3 or more AEDs group against single or 2 AEDs group. *s.d.* : standard deviation, **p*-value < 0.05 is significant

most patients were on either on one (12.50% of patients) or two (11.25% of patients) AEDs. The maximum number of AEDs taken was noted to be 4, with 3 patients (3.75%) were on 4 AEDs concurrently. It was statistically significant that there is an increased risk of suicidal ideation in patients on 3 or more AEDs compared to patients taking 1 or 2 types of AEDs ($M=1.38$, 95%CI [1.08, 1.69], $p=0.016$). Patients with epilepsy occurring on a daily to weekly basis has significantly higher tendency to have suicidal ideation (33.33%) ($p=0.004$). No statistical differences were noted in the group of patients with seizures occurring every monthly or less. In the univariate analysis, previous head surgery, number of AEDs, seizure frequency and BDI-II score were noted to be statistically significant. Upon multiple logistic regressions, the above covariates did not show any significance.

On the C-SSRS, 21 out of 27 patients of suicidal epilepsy patients were noted to have the less severe form of suicidal ideation. On the categories of C-SSRS, non-specific active suicidal thoughts were the majority at 16.25% followed by

wish to die at 10.00% and active suicidal ideation with any methods without intent at 6.25%.

The BDI-II score was statistical significantly higher in the suicidal ideation group (13.48 ± 6.48) compared to the non-suicidal group (6.85 ± 5.26) ($p < 0.001$) in Table 4. In the suicidal group, the majority was in the mild mood disturbance group (12.50%) followed by borderline clinical depression group at 18.75% and 5% in the severe depression group. The difference of BDI-II score in both groups was statistically significant with a p-value of less than 0.001.

DISCUSSION

Multiple studies had been conducted to ascertain the effects of epilepsy both as a condition and a disease itself to the patient. There is a well-known correlation between epilepsy and depression with previous studies showing 11-65% of epilepsy patients suffering from depression.^{12,13} Epilepsy in itself may cause and increase the risk of depression. A vicious cycle, several studies have shown a bi-directional cause and effect between depression and epilepsy.¹⁴⁻¹⁷ Therefore, depression

Table 4: Beck's Depression Inventory-II (BDI-II) and Columbia Suicide Severity Rating Scale (C-SSRS) category of epilepsy patients with suicidal ideation and non-suicidal ideation

Characteristics	Suicidal ideation	Non-suicidal	p-value
Beck's Depression Inventory Score			
Mean (\pm s.d.)	13.48 (± 6.48)	6.85 (± 5.26)	< 0.001 *
Beck's Depression Inventory Category, n (% of total)			
- Minimal	16 (20.00)	46 (57.50)	< 0.004*
- Mild	6 (7.50)	5 (6.3%)	
- Moderate	5 (6.30)	2 (2.50)	
Severity of suicidal ideation, n (%)			
No suicidal ideation	0 (0.00)	53 (66.25)	<0.001
Less severe	21 (26.25)	0 (0.00)	
Severe	6 (7.50)	0 (0.00)	
C-SSRS score, n (%)			
- No suicidal ideation	0 (0.00)	53 (66.25)	
- Wish to die	8 (10.00)	0 (0.00)	
- Non specific active suicidal thoughts	13 (16.25)	0 (0.00)	
- Active suicidal ideation with any methods without intent	5 (6.25)	0 (0.00)	
- Active suicidal ideation with some intent	0 (0.00)	0 (0.00)	
- Active suicidal ideation with specific plan and intent	1 (1.25)	0 (0.00)	

p-value calculated using Pearson's Chi Square, with exception of θ calculated by independent t-test and \dagger by Yates' correction

*s.d. : standard deviation, *p-value < 0.05 is significant*

itself in turn may be the trigger and may reduce the threshold of seizure. Of the whole spectrum of depression in epilepsy, the most worrying and stressing component would be suicidal ideation or the completed suicide event itself.

Studies of prevalence of suicidal ideation in epilepsy patients have been reported as high as 36.7% in certain populations.⁵ This is contrast to the prevalence of 1.0-1.4% in the general population. Not only do epilepsy patients have higher tendency for suicidal ideation; but the type of epilepsy itself such as temporal lobe epilepsy carries a higher risk; up to 6-25 fold risk of suicidal ideation^{18,19}, whereas complex partial seizure was noted to have up to a 25 fold increase risk of suicide.^{14,20}

On socio-cultural aspect, majority of epilepsy patient faces negative stigmata associated with suicide and find employment difficulties; which subsequently leads to financial difficulties. This is evident especially in the Asian countries where poor social support and the social stigma associated with epilepsy thus rendering epilepsy patients to face isolation from the community. Disease complications and activity restrictions with the negative social stigmata attached to epilepsy would have increased pressure on the affected individuals and family members. Furthermore, AEDs presents as an easy access to facilitate suicide as it leads to mortality when taken at high dosages.

The presence of mood disorder is the single most important risk factor for suicide in epilepsy patients. It has been reported in several studies that depression not only affects the quality of life but is also a predictor for suicidal ideation in epilepsy patients.¹⁻⁴ It has been reported that 11-65% of epilepsy patients suffers from depression. Our study showed that the epilepsy group has a significantly higher tendency for depression at a mean BDI-II score of 9.09 ± 6.48 compared to the control group 5.56 ± 4.56 which are in keeping with similar findings of previous studies.²¹⁻²³ The category of depression is also more severe comparatively as the epilepsy group has a higher tendency for mild mood disturbance, borderline clinical depression and moderate depression. The association between depression and epileptic seizures shows a bi-directional relationship at which depression itself could induce an epileptic seizure while recurrent seizure episodes, intra-ictal and post-ictal psychosis may lead to the development of depression.²⁴ Factors contributing to development of depression in epilepsy patients had been studied extensively previously and these

factors include but not limited to epileptic type, seizures frequency, isolation from occupational and social activities and the stigmata associated to epilepsy.²⁵

Generalised convulsive seizure is the most common type of epilepsy in both epilepsy patients group with suicidal ideation (18.75%) and in epilepsy patients with no suicidal ideation (41.25%). This is followed by complex partial seizures in both suicidal (12.50%) and non-suicidal epilepsy patients group (16.25%). This is in contrast with our literature review, which emphasized that complex partial seizure is the one most commonly associated with suicidal ideation.^{14,20,26} Plausible explanation could be due to generalized convulsive seizure is by far the most common seizure type in Malaysia. A previous meta-analysis on the epidemiology of epilepsy in Asia showed 86.0 - 92.0% of epilepsy in Malaysia are due to generalized seizure as opposed to 8.0 - 14.0% partial seizures.²⁷⁻²⁹ The sheer difference in frequency of these two types of epilepsy would explain as to why there were less than anticipated complex partial seizure patients in the suicidal ideation group.

Eight out of the 12 (66.66%) subjects who have had brain surgery had significantly higher rate of suicidal ideation. The positive correlation is in keeping with previous studies and highlights the need for the treating physician to aware of the markedly increased risk of suicidal ideation in post surgery epilepsy patients.^{15,30,31}

In the treatment of epilepsy, most often the aim of treatment is to have the most minimum occurrence of epileptic seizure on the most minimum AEDs or medication. Therefore, there are few instances at which an uncontrolled epilepsy patient will require more than one AED. 58.75% were on only one AED, 25.00% on 2 AEDs, 12.50% on 3 AEDs and 3.75% on 4 AEDs. Upon comparison of suicidal ideation epilepsy patients and non-suicidal ideation epilepsy patients, it showed a significant result at which those with suicidal ideation are the patients who are on more three or more AEDs. There were no differences in risk in patients taking one or two AEDs. This is in agreement with other studies that noted AEDs polypharmacy is a risk factor for suicidal ideation.^{14,15,32} Our study did not find any association or correlation between any particular or specific AED and suicidal ideation.

Generally, it is acknowledge that AED with positive GABA properties causes a decrease in serotonin secretions and negative psychotropic effect and therefore, increase the risk of

depression and suicidality. These GABA positive AED includes benzodiazepines, topiramate and gabapentin. Other AEDs such as phenobarbitone, lamotrigine and levetiracetam has also been link to an increase in suicide risk.³³

Valproate has been shown to be a mood stabiliser and used in other psychiatric conditions such as bi-polar disorder and major depressive disorders. However, valproate as a mood stabilizer has not been proven in epilepsy patients as these previous studies were based on studies in bi-polar and comparing to the lithium, the gold standard in bi-polar therapy.^{34,35} Similarly, lamotrigine were also deemed to have a protective effect but again, the studies were on bi-polar subjects with no formal clinical trial on epilepsy patients.³⁴⁻³⁷ This is also in contradictory statement to other papers linking lamotrigine to an increase in suicide risk.^{33,34} Carbamazepine on the other hand has been shown to have a mood stabilizing effect with a study showing a negative correlation with suicidality in female patients.^{36,38}

We did not find any significant increase risk of suicidal ideation in comparison with the various types of AEDs. However, we confirmed that AED's polypharmacy does increase the risk of suicidal ideation, consistent with previous studies.^{14,15,32} Our findings are in agreement with several studies and meta-analysis, which disputes the FDA warning on suicidality and AEDs.^{6,34,39-42}

This study supports published reports from the western hemisphere and Japan in that there is a higher risk for suicidal ideation in epilepsy patients. The proportion of suicidal ideation is present in 33.75% of the epilepsy patients in our setting. There is an increased risk of 9.68 times to develop suicidal ideation. Factors were shown to be associated with suicidal ideation in epilepsy patients include previous head surgery, polypharmacy, depression (higher BDI-II scores) and uncontrolled epilepsy with higher seizure frequencies. Early recognition of high-risk epilepsy patients and timely referrals to the psychiatry unit is of paramount importance in the management of epilepsy.

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DISCLOSURE

Conflict of interest: None

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