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Depression, anxiety and suicidal ideation/behaviour among persons with epilepsy: Common but underestimated comorbidities in Haryana, North India

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Abstract

Background & Objectives: Depression, anxiety and suicide are the main psychiatric comorbidities which are more prevalent among persons with epilepsy (PWE). This study aims to determine the prevalence of depression, anxiety and suicidal ideation/behaviour in PWE and to correlate their clinical profile with psychiatric comorbidities in a population in North India. *Methods:* This study was conducted at Pt. BD Sharma PGIMS, Rohtak Haryana among PWE attending outpatient clinic at the Department of Neurology. A total of 100 eligible PWE were included in this study. The demographic and clinical history was documented. All patients filled up the Hospital anxiety and depression scale (HADS) and Columbia-suicide severity rating scale (C-SSRS) questionnaire. *Results:* The prevalence of depression and anxiety among PWE was found to be 60% and 70% respectively and the prevalence of suicidal ideation and suicidal behaviour was 42% and 3% respectively among PWE. Female gender, longer duration of epilepsy, higher seizure frequency, temporal lobe epilepsy, polytherapy, uncontrolled epilepsy and drug resistant epilepsy were found to be positively correlated with these psychiatric comorbidities. *Conclusion:* This study shows that the prevalence of depression, anxiety and suicidal ideation/ behaviour is high among PWE in Haryana, North India. PWE should be screened for these psychiatric comorbidities to improve their quality of life.

Keywords: Epilepsy; Psychiatric comorbidities; Risk factors

INTRODUCTION

Epilepsy is the second most common neurological disorder characterised by recurrent unprovoked seizures. The incidence of epilepsy in low-income countries may be as high as 190 per 100 000 people.[1] India is home to about 10 million person with epilepsy (PWE) with prevalence of about 1%, this being higher in the rural (1.9%) as compared with the urban counterpart (0.6%).[2] Epilepsy is associated with increased risk of psychiatric disorders, although incidence and prevalence rates of psychiatric comorbidities vary widely among studies, from 12 to 41%.[3] Psychiatric symptoms in PWE could be related to seizure itself (peri-ictal) or independent of seizure occurrence (inter-ictal). The psychiatric comorbidities reported in PWE include psychoses, neuroses, mood disorders, personality disorders and behavioural problems. Depression, anxiety and suicidal ideations are frequent among PWE. The risk factors are not well determined. It is vitally important for the physicians treating PWE to recognise the symptoms of coexisting psychiatric disorders among PWE. As the effective recognition and treatment of psychiatric comorbidities may improve their quality of life. This study was conducted to evaluate the prevalence of depression, anxiety, suicidal ideation/ behaviour in PWE coming to our tertiary care centre in Haryana, North India. The secondary objectives were to assess correlation between their clinical profile and psychiatric comorbidities.

METHODS

In this study, 100 persons aged 18 and above with a confirmed clinical diagnosis of epilepsy (who have been diagnosed and under treatment for more than a year) and had generalised tonic clonic seizures were included in the study over a period of 6 months. The epilepsy patients who attended the outpatient Neurology Department were enrolled consecutively in the study.

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Sample size calculation

Jacoby *et al*[9] reported that prevalence of anxiety and depression in epileptic subjects was 25% and 9% respectively. Taking this value as reference, the minimum required sample size with 9% margin of error and 5% level of significance was 89 patients. To reduce margin of error, total sample size taken was 100. The formula used was:- $N \geq (p(1-p))/(ME/z_{\alpha})^2$, where Z_{α} is value of Z at two-sided alpha error of 5%, ME was margin of error and p is prevalence rate. Thus, for anxiety, $n \geq ((.25*(1-.25))/(.09/1.96)^2 = 88.92 = 89$(approx.). For depression, $n \geq ((.09*(1-.09))/(.09/1.96)^2 = 38.84 = 39$(approx.)

Patients with history of seizure in the last thirty days, substance or alcohol abuse, patients with any work related disability arising out of the cause of seizure like post stroke seizure causing motor dysfunction, ongoing chronic medical illnesses like diabetes, hypertension, chronic renal disease, psychiatric disorders antedating the onset of seizures, psychiatric comorbidities other than depression, anxiety and suicidal ideation/ behaviour and significant cognitive dysfunction (MMSE <24) were excluded from the study. After obtaining an informed consent, detailed demographic history and clinical history of epilepsy was taken. All study subjects filled up the following questionnaires: Hospital Anxiety and Depression (HADS) scale for assessment of depression and anxiety and Columbia-Suicide Severity Rating Scale (C-SSRS) for Suicidal ideation and behaviour. The HAD scale consisted of 14 items, measuring anxiety and depression on two separate subscales, each consisting of 7 items. There were four response categories, from 0 to 3 to each item with a maximum total for each subscale of 21. In the ongoing treatment for epilepsy, "control of epilepsy" was taken as 1 year without seizure on antiepileptic drugs; and "drug resistant epilepsy" were those who despite the use of two appropriately chosen antiepileptic drugs in an optimal doses, seizure was not controlled in the past one year. The patients were categorized as "Controlled" if they were free of all types of seizures for one year while on treatment whereas they were labelled as "Uncontrolled" if they had ≥ 1 episodes of seizures in the past one year while on treatment.

Statistical analysis

Categorical variables were presented in number and percentage (%) and continuous variables were presented as mean ± SD. Qualitative variables were correlated using Chi-Square test/Fisher's exact test. After applying Bonferroni correction, p value of <0.006 was considered statistically significant. The data was entered in MS EXCEL spreadsheet and analysis was done using Statistical Package for Social Sciences (SPSS) version 21.0.

RESULTS

A total of one hundred PWE filled out the questionnaires. The majority of patients were within 18-25 years of age with a mean age of 26.87±8.27 years, there were more males (n=70). About half belonged to middle class, followed by lower and upper class i.e. 49%, 30% and 21% respectively (using Kuppuswamy scale). Out of a hundred patients, 73 patients had idiopathic/cryptogenic epilepsy and 27 patients had symptomatic epilepsy comprising of Neurocysticercosis (n=16), mesial temporal lobe sclerosis (n=7), tuberculoma (n=2), gliosis (n=1), and focal cortical dysplasia (n=1). Mean age at onset and duration of epilepsy were 18.87±7.79 year and 8±6.01 year respectively. Thirty seven percent of patients were on monotherapy and 63% on polytherapy. Demographic and clinical profile are shown in Table 1.

For the Hospital Anxiety and Depression Scale (HADS), 60% of patients scored more than seven on HADS-D with a mean of 7.77±3.25, and 70% of patients scored more than seven on HADS-A with a mean score of 9.03±3.95. On assessment by C-SSRS, 42% of patients were found to have suicidal ideation/thoughts and 3% of patients had suicidal behaviour. Figure 1 shows the overall prevalence of psychiatric comorbidities among the PWE.

Female gender had a significantly higher association of depression; however age as categorised into ≤25 and >25 years, was comparable. Among other factors analysed, polytherapy, uncontrolled epilepsy, and drug resistant epilepsy had significantly higher depression, anxiety and suicidal behaviour. (P<0.05) It was also found that temporal lobe epilepsy (TLE) had higher depression and anxiety as compared to non-TLE patients. (Table 2)

DISCUSSION

This was a cross-sectional study conducted among PWE to determine the prevalence of psychiatric co-morbidities and its correlation with their demographic and clinical profile.

The prevalence of depression and anxiety among PWE was found to be 60% and 70%

Table 1: Demographic and clinical details of persons with epilepsy (n=100)

Age(years)	26.87±8.27(mean ± SD)
Sex Male Female	No. of patients(n) 70 30
Marital Status Married Unmarried	No. of patients(n) 51 49
Socioeconomic status Lower class Middle class Upper class	No. of patients(n) 30 49 21
Age at onset of seizure(years)	18.87±7.79(mean ± SD)
Duration of epilepsy(years)	8±6.01(mean ± SD)
Epilepsy Type Idiopathic epilepsy Symptomatic	No. of patients(n) 73 27
Number of AEDs Monotherapy Polytherapy	No. of patients(n) 37 63
Seizure Control Controlled Uncontrolled	No. of patients(n) 44 56

respectively and the prevalence of suicidal ideation and suicidal behaviour was 42% and 3% respectively. This was higher than the results from a meta-analysis by Lawrence *et al*. where the prevalence of depression, anxiety, suicidal ideation/suicidal behaviour in various studies has been found to be 11-80%, 15-25% and 2-9.1% in PWE as compared to 3.3%, 5.1-7.2% and 1%

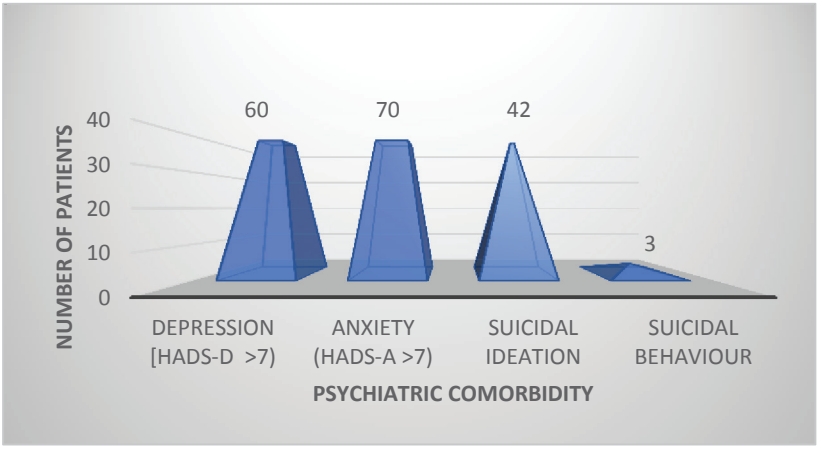

Figure 1. Overall prevalence of psychiatric comorbidities in persons with epilepsy (n=100)

Table 2: Correlation between prevalence of psychiatric comorbidities and clinical profile of persons with epilepsy

Clinical Parameter	Depression n (%)	Anxiety n (%)	Suicidal ideation n (%)	Suicidal behaviour n (%)
Age at onset				
≤25years (n=81)	48(59.26%)	58(71.60%)	33(40.74%)	3(3.70%)
>25years (n=19)	12(63.16%)	12(63.16%)	8(42.11%)	0(0.00%)
	(p =0.958*)	(p =0.656*)	(p =0.88*)	(p =1#)
Gender association				
Male(70)	35(50.00%)	48(68.57%)	23(32.86%)	0(0.00%)
Female(n=30)	25(83.33%)	22(73.33%)	18(60.00%)	3(10.00%)
	(p =0.004*)	(p =0.812*)	(p =0.021*)	(p =1#)
Duration of Epilepsy (years)				
≤5(n=46)	23(50.00%)	28(60.87%)	13(28.26%)	2(4.35%)
>5(n=54)	37(68.52%)	42(77.78%)	28(51.85%)	1(1.85%)
	(p =0.093*)	(p =0.105*)	(p =0.029*)	(p =0.593#)
Type of Epilepsy				
Symptomatic (n=27)	14(51.85%)	17(62.96%)	13(48.15%)	0(0.00%)
Idiopathic epilepsy (n=73)	46(63.01%)	53(72.60%)	28(38.36%)	3(4.11%)
	(p =0.434*)	(p =0.491*)	(p =0.512*)	(p =0.561#)
Number of AEDs				
Monotherapy(n=37)	13(35.14%)	19(51.35%)	7(18.92%)	0(0.00%)
Polytherapy(n=63)	47(74.60%)	51(80.95%)	34(53.97%)	3(4.76%)
	(p =.0002*)	**(p =.004*)**	**(p=.001*)**	(p =0.294#)
Control of Epilepsy				
Controlled(n=44)	15(34.09%)	23(52.27%)	7(15.91%)	0(0.00%)
Uncontrolled(n=56)	45(80.36%)	47(83.93%)	34(60.71%)	3(5.36%)
	(p <0.001*)	**(p =0.001*)**	**(p <0.001*)**	(p =0.253#)
Drug Resistant Epilepsy				
Yes(n=45)	39(86.67%)	40(88.89%)	30(66.67%)	3(6.67%)
No(n=55)	21(38.18%)	30(54.55%)	11(20.00%)	0(0.00%)
	(p <0.001*)	**(p =.0004*)**	**(p <0.001*)**	(p =0.088#)
TLE patients (n=15)	14(93.33%)	15(100.00%)	9(60.00%)	0(0.00%)
Non-TLE patients (n=85)	46(54.12%)	55(64.71%)	32(37.65%)	3(3.53%)
	(p <0.004#)	**(p =0.004#)**	(p =0.181*)	(p =1#)

*-Chi square test; #-Fisher's Exact test; AED: Anti-epileptic drugs, TLE: Temporal lobe epilepsy

respectively in general population.[4] It was also higher than the results of a study by Tellez-Zenteno *et al*. using data from the Canadian Community Health Survey, with administration of the World Mental Health Composite International Diagnostic Interview (CIDI), that found a lifelong psychiatric disorder diagnosis in 35% of PWE, compared with 20% of non-epileptic individuals.[5] Our study was also higher than a study from North East India, where psychiatric comorbidity was seen in 50% subjects with epilepsy. The common psychiatric morbidities reported in the study were depression, psychosis and anxiety disorders (18%, 14% and 11% respectively).[6]

In a systematic search for articles published from India from 2006-2016, comorbidities in epilepsy were found to be integral part of PWE partly due to poor awareness among patients, families, and treating physicians. The high prevalence of comorbidities further complicates the ongoing management and call for the treating physicians to assess for all associated co-morbidities, in addition to psychiatric, including migraine, cognitive impairment and mortality.[7] In another community-based Indian sample of 976 adults with active epilepsy who answered a questionnaire, high depression scores were found in the study population.[8] In another study conducted on paediatric population in Kerala, India, screening questionnaires and interviews with caregivers and teachers showed significant issues impacting the psychological well-being of the children and caregivers.[9]

It has been shown that depressive symptoms not only arise after the onset of epilepsy but is also seen before the seizure onset, suggesting a complex plethora of changes in the neurotransmitters that occur in epilepsy, and other psychiatric disorders like depression and anxiety.[7]

The demographic profile such as age, marital status and socioeconomic status of PWE in this study were non-significantly associated with depression, anxiety and suicidal ideation/ behaviour except for female gender which was significantly associated with depression in the study group. A study by Kimiskidis *et al*. also found significant association between female gender and depression in PWE.[10] Clinical profile such as age at onset of epilepsy and type of epilepsy were not significantly associated with psychiatric comorbidities in our study. This concurs with a study by Vujisic *et al*. who found no statistically significant correlation between age of onset of seizure and psychiatric comorbidities.[11] A study by Filho et al. found high prevalence of depression and anxiety in both groups with focal (41%) and generalized (46.7%) seizures, but no statistically significant difference between two groups.[12] Previous Indian studies also found no association of onset of seizure with psychiatric co-morbidities.[6,7]

In our study, duration of epilepsy had no significant association with depression and anxiety. Study by Kimiskidis *et al*.[10] also found no statistically significant correlation between duration of seizure disorder and increased prevalence of depression and anxiety. However, Rehman[6] reported an association of long duration of epilepsy with presence of psychiatric comorbidity in PWE. Also we found that the prevalence of psychiatric disorders was higher in persons with uncontrolled seizures. Similarly, a study by Jacoby *et al*., 21% of persons with uncontrolled seizures were depressed as compare to 9% with controlled seizures.[13] Our study showed that PWE on two or more AEDs had higher prevalence of psychiatric disorders. In the study by Vujisic *et al*., 72.72% of persons on polytherapy were depressed as compared to only 15.38% of PWE on monotherapy (p=0.05).[11] The intake of two or more AED and poor compliance associated with multiple medicines was found to have a negative impact on the psychiatric condition of the patients as reported by a tertiary hospital in Delhi (India).[6]

TLE and drug resistant epilepsy were also positively associated with depression and anxiety in the present study. Similarly, using Becks depression inventory (BDI), Quiske *et al*. found that PWE with TLE had worse score when compared to non-TLE patients.[14] Another study by Hitiris *et al*. found that depression alone accounted for 85% of psychiatric disorder among persons with drug resistant epilepsy (odds ratio 2.27; p=0.001).[15]

The association of depression and anxiety with multiple AED therapy, drug resistant therapy, and uncontrolled epilepsy can be due to the side effects of AED. The stigma associated with epilepsy in India can be an additional factor leading to decreased social mobility contributing to depression. The social outcast, family ignorance and burden, decreased work efficiency, fear of having an attack in the public at any time may be other factors for increased prevalence of anxiety and depression in our study patients. The association of TLE with increased anxiety and depression can also be related to the perception by the PWE that the temporal lobe lesions being more serious. This indicates the need for counselling

for such patients about the disease with referral to the psychiatric service for further evaluation and intervention to provide a more comprehensive care to the patients.

The limitations of this study are firstly, the methodology of the study suffered from the major limitation of assessing the prevalence of depression, anxiety and suicidal ideation based on HADS scale and self-made questionnaire rather than ICD criteria. Thus the results cannot be interpreted against the population prevalence. Secondly, there may be a relation between specific AEDs and psychiatric comorbidities, but this was not studied in the study. Thirdly, due to inclusion of patients with only GTCS, the sampling population showed higher number of patients with idiopathic epilepsy. Lastly, though we referred all patients with anxiety or depression to the psychiatric department for further intervention, the follow-up of such patients was not done. Thus we recommend that future studies should have long term follow up of the psychiatric intervention and side effects of AED as psychiatric co-morbidities in epilepsy patients.

In conclusion, the overall prevalence of depression, anxiety and suicidal ideation was 60%, 70% and 42% respectively in a cohort of PWE in Haryana, North India. Significant risk factors identified were female gender, TLE, polytherapy, uncontrolled epilepsy and drug resistant epilepsy. All PWE should be screened for psychiatric comorbidities especially in persons with above mentioned risk factors.

DISCLOSURE

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Conflicts of interest: None

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