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Original Research Article

Cross sectional study to determine the cognitive impairment among epilepsy patients

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ABSTRACT

Background: The study was aimed to screen cognitive impairment and assess its levels among epilepsy patients, also study the prevalence and the relationships between specific seizure subtype and determine the correlation between seizure frequency, seizure duration and abnormal EEG finding with cognitive impairment among epilepsy patients.
Methods: The study was conducted in a tertiary care hospital over a period of 1yr after taking informed consent from 100 patients by random sampling after fulfilling the inclusion criteria.
Results: Out of 100 patients 64% did not have cognitive impairment, 36% had cognitive impairment. Among 36%, 7% had definitive cognitive impairment and 29% had mild cognitive impairment. It was observed that the other group of seizure subtypes which included atonic, myoclonic, focal sensory, focal motor, absence seizure with secondary generalization had low mean cognitive scores signifying cognitive impairment, where as those with complex partial seizure with secondary generalization group had high mean cognitive scores signifying no cognitive dysfunction. However, the observed difference is statistically significant ($p<0.05$). Patients who had higher seizure frequency had low mean cognitive scores indicating cognitive decline and those with very low seizure frequency had high mean cognitive scores indicating no cognitive decline. However, the observed difference is statistically significant. It was observed that the mean cognitive score for abnormal EEG patients was 24.68 indicating mild cognitive decline whereas for normal EEG patients the mean cognitive score was 26.27 indicating no cognitive decline however the observed difference is statistically significant since $P<0.05$.
Conclusions: The high prevalence of cognitive impairment among epilepsy patients calls for early neuropsychological assessment soon after the diagnosis of epilepsy beyond that, the baseline screening may also guide treatment plan and serve as an early indicator for rehabilitative care.

Keywords: Cognitive impairment, Cognition, Complex partial seizure, Epilepsy, Seizures

INTRODUCTION

Epilepsy is a chronic disorder manifested by recurrent, often erratic seizures which may be disconcerting and troublesome to the normal commotion of daily living affecting people of all ages. Approximately 50 million people worldwide have epilepsy, making it one of the most common neurological diseases globally nearly 80% of the people with epilepsy live in low and middle-income countries. In India there is very little data available among psychiatric morbidities amongst seizure disorders. Irrespective of the socioeconomic status and gender discrepancies all ages of epilepsy patients suffer from psychiatric morbidity. People with epilepsy respond to treatment approximately 70% of the time. About three fourths of people with epilepsy living in low- and middle-income countries do not get the treatment they need. In many parts of the world, people with epilepsy and their

families suffer from stigma and discrimination.[1] Temporal lobe epilepsy (TLE) is the most frequent form of focal epilepsy in adult i.e. about 80%, neuropsychological scores worsen with advanced age, long duration of epilepsy, high seizure frequency, Anti-epileptic drugs (AED'S) and presence of temporal lesion on cerebral MRI. However, high level of education seems to be protective.[2] Psychiatric co-morbidities are more common among unmarried, unemployed, people living from rural background, it is also more among people taking multiple AED'S.[3] Epilepsy can be complicated by neurobehavioral co morbidities, which include cognitive impairment, psychiatric disorders, and social problems. Although such comorbidities are traditionally thought to arise predominantly from the effects of recurrent seizures and AED'S. Other possibilities like altered neurodevelopment of the brain, acceleration of common age-associated changes and negative treatment effects should also be considered leading to uncertain and understudied outcome in old age.[4,5] Recent studies suggest that common symptoms among cognitive decline were impairment of either verbal or figural memory and letter based verbal fluency in TLE.[6,7] Cognitive and behavioral involvement is the rule, not the exception, among patients with disorders of the central nervous system (CNS).[8] Cognitive impairment in person leads to difficulty in performing daily day today activities, such individuals may complain of impaired attention, word-finding difficulty, verbal fluency difficulty, forgetfulness and psychomotor slowing. Memory disturbance being the most common symptom among them. Such individuals may rely on smart phones to check the dates calculate and set reminder notes and somehow accomplish all their customary tasks independently. Mild cognitive impairment is associated with a higher than normal risk of developing dementia of Alzheimer's type.[9,10] Harmful effects of AED's include aggression, impaired cognition, attention difficulties, depression, irritability, sexual dysfunction, confusion and sleep disturbances.[11] Cognitive impairment is less among newer AED's and people adhering to single drug regimen whereas cognitive impairment is more with patients on polytherapy.[12] Phenobarbital and topiramate have known to cause more cognitive impairment.[13] In the recent SANAD study patients with newly diagnosed but not yet treated epilepsy as well as healthy controls participated in a battery of neurocognitive tests even prior to initiating treatment, cases scored relatively worse compared to controls so these findings suggest that subtle cognitive impairments likely preceded the onset of epilepsy as these patients had only had a few seizures at the time of testing.[14] Many of the neuropsychological scales and tests are of limited use for general practitioners (GPs) to detect cognitive impairment. Mini-mental state examination (MMSE) is a simple screening tool which detects dementia at the earliest and can be easily administered by GPs.[15-21]For the practicing clinician, perhaps the most important message to remember is that there is no such thing as "just epilepsy." Any patient with epilepsy should be viewed as someone who is at risk of encountering a variety of consequences including cognitive difficulties, behavioral disorders, depression, suicide, and also sudden death. There is absolutely no reason to re-stigmatize epilepsy, but there is every reason to make sure physicians, patients, families, as well as educators and others are adequately prepared to recognize any such difficulties and to manage them appropriately.[22]As for the treatment of TLE early detection and seizure control is more important in preventing developmental disability in early childhood and accelerated progression of cognitive decline with ageing.[23] When cognitive issues are not addressed adequately, the morbidity of these patients may increase and this may interfere with the epilepsy treatment adherence. So present study was aimed to screen for cognitive impairment and to assess the level of cognitive impairment among epilepsy patients, to study the prevalence and the relationships between specific seizure subtype and to determine the correlation between seizure frequency, seizure duration and abnormal EEG finding with cognitive impairment among epilepsy patients.

METHODS

Hundred patients (52 males, 48 females) aged between 16-50 years visiting the outpatient Department of Psychiatry were randomly recruited for the study. A written informed consent was taken from all the individuals after being advised about the nature of the study according to a protocol approved by the Ethics Committee of Sambhram Institute of Medical Science and Research, KGF, Kolar, Karnataka, India.

Inclusion criteria

Patients with evidence or history of epilepsy and on treatment and whose last seizure episode was more than seven days were included in the study.

Exclusion criteria

- Patients with other co-morbid physical illnesses such as diabetes, hypertension, ischemic heart disease, hypothyroidism,
- Patients with known psychiatric illness before the onset of epilepsy,
- Un-cooperative patients and who refused to participate in the research and give informed consent for assessment excluded from this study.

A semi structured proforma comprising of personal, sociodemographic profile diagnosis, EEG and radio imaging findings, seizure duration, frequency, drug history, compliance, family history, and other relevant details necessary for the study design was used. Semi structured proforma, MINI Plus neuropsychiatric interview and mini mental status examination (MMSE) were used. MINI plus neuropsychiatric interview is a short structured clinical interview which has 20 separate modules for each disorder and is used to diagnose axis I

disorders according to DSM V or ICD 10 developed by Sheehan et al. It has been validated and reliability has been studied in comparison to the SCID-P (abbreviated as structured clinical Interview for DSM V) and the CIDI (composite international diagnostic interview) which is a structured discussion established by the world health organization for untrained interviewers for ICD-10. It has a high inter-rater reliability and validity. It is a clinician administered scale and can be completed within 15 minutes. M.I.N.I. Plus is allocated into modules recognized by letters with each letter agreeing to a diagnostic category. There are screening questions corresponding to the main criteria at the commencement of each diagnostic component except for psychotic illness.

Diagnostic box at the end of each module is given to indicate whether diagnostic criteria are met or not. Mini-mental state examination (MMSE) or The Folstein test is a thirty-opinion inquiry form introduced by Folstein et al, used as a detective tool for cognitive impairment. It is very often used to detect dementia in addition to evaluate the depth of cognitive decline and to track the sequence of cognitive decline in patients over time and serves as an effective way to monitor a person's reaction to treatment. It is operational as a detecting tool aimed at cognitive impairment with old age, hospitalized adults.

It is also used as an exploration instrument for screening cognitive decline in epidemiological works and follows cognitive variations in clinical trials. It has 11-questions which measures 5 zones of cognition including orientation, registration, attention, and calculation, recall and language.

Extreme tally is 30, a score of 23 or lower is indicative of cognitive impairment. It takes around 10 minutes to administer and is easy to use repeatedly and routinely. It relies primarily on verbal response and reading and writing and as a result certain group of people performs poorly even when their cognition is intact. They include patients who are blind and deaf, intubated, have low English literacy or those with other communication disorders.

Statistical analysis

Statistical analysis was performed using SPSS v15.0 statistical package (SPSS Inc., IL, Chicago USA). Descriptive analysis was performed to statistically demonstrate the correlation between different measurements. Student t test and F test was used to compare different variables.

RESULTS

The results demonstrated that out of 100, 52 % were females and the remaing 48% were males. 24% were below 26 years, 51% were from 27 to 37 years and the remaining 25 percent were above 38 years. Majority that is 42% were of primary grade literacy profile and next common was high school 27%.

Regarding the occupation majority belonged to unskilled group of workers and housewife's which constituted 23%. Regarding marital status 77% of them were married and only 17% of them were unmarried. Majority belonged to lower, upper lower and lower middle socio-economic status.

Regarding the type of family in which they were living, 65% of them were from nuclear family and the remaining 35% was joint family type. It was found that 56% of epileptic patients had abnormal EEG findings and the remaining 44% had normal EEG.

Regarding drug compliance, 59% had good compliance and 26% patients had average compliance and 15% had poor compliance. It was found that majority of the participants for the study group were from GTCS which constituted 34%. complex partial seizure with secondary generalization were 23%, focal motor seizure with secondary generalization were 17%, complex partial seizure was 14% and others were 12%. Regarding grades of cognitive decline, 36% had cognitive impairment out of which 7% had definitive impairment and 29% had mild impairment (Table 1).

Table 1: Prevalence of cognitive decline among different seizure type.

Psychiatric morbidity	GTCS	CPS	CPSWSG	FMSWSG	Others	Total
COG impair	11	6	5	6	8	36

It was observed that the other group of seizure subtypes which included atonic, myoclonic, focal sensory, focal motor, absence seizure with secondary generalization had low mean cognitive scores signifying cognitive impairment, where as those with complex partial seizure with secondary generalization group had high mean cognitive scores signifying no cognitive dysfunction. However, the observed difference is statistically significant, since the F ratio is significant at 0.05 level (Table 2).

Those who had longer seizure duration more than 16 years and above had cognitive decline since their mean scores were low. It was also observed that those who had seizure duration between 6 to 10 years had high mean scores indicating no cognitive decline. However, the observed difference is not statistically significant, since

the F ratio is not significant at 0.05 level (Table 3). It was observed that those who had higher seizure frequency had low mean cognitive scores indicating cognitive decline and those with very low seizure frequency had high mean cognitive scores indicating no cognitive decline.

Table 2: Distribution of samples based on seizure type vs cognitive impairment.

Seizure duration in years	Cognitive impairment			N	Mean	SD	F ratio	Significance
	Absent	Mild	Definite					
GTCS	23	10	1	34	25.74	3.621	4.501	0.002* P<0.05S
CPSWSG	18	5	0	23	26.61	2.210		
FMSWSG	11	5	1	17	25.35	2.849		
COMPLEX	8	5	1	14	25.50	3.252		
Others	4	4	4	12	21.92	3.801		
Total	64	29	7	100	25.38	3.408		

Table 3: Distribution of samples based on seizure duration vs cognitive impairment.

Seizure duration in years	Cognitive impairment			N	Mean	SD	F ratio	Significance
	Absent	Mild	Definite					
<5	17	6	1	24	25.79	2.502	2.507	0.064 P>0.05NS
6 to 10	26	9	2	37	26.16	3.633		
11 to 15	13	4	3	20	25.05	3.748		
16 and >	8	10	1	19	23.68	3.163		
Total	64	29	7	100	25.38	3.408		

P >0.05, * Significant

Table 4: Distribution of samples based on seizure frequency vs cognitive impairment.

Seizure frequency (per year)	Cognitive impairment			N	Mean	SD	F ratio	Significance
	Absent	Mild	Definite					
Below 1	28	8	0	36	26.94	2.787	21.610	0.000* P<0.05S
2-5/ years	31	10	0	41	25.88	2.282		
5and above	5	11	7	23	22.04	3.784		
Total	64	29	7	100	25.38	3.408		

P <0.05, * Significant

Table 5: Distribution of samples based on EEG VS cognitive impairment.

EEG	Cognitive impairment			N	Mean	SD	t	Sig.(2-tailed)
	Mild	Definite	Absent					
Abnormal	32	19	5	56	24.68	3.644	-2.376	0.019*
Normal	32	10	2	44	26.27	2.880		
Total	64	29	7	100	25.38	3.408		

P <0.05, * Significant

However, the observed difference is statistically significant, the F ratio is not significant at 0.05 level (Table 4). It was observed that the mean score for abnormal EEG patients was 24.68 indicating mild cognitive decline whereas for normal EEG patients the mean cognitive score was 26.27 indicating no cognitive decline. However, the observed difference is statistically significant since P<0.05 (Table 5).

DISCUSSION

The study using a cross sectional design examined and estimated the prevalence of cognitive impairment among the epilepsy patients. The findings in the study bring to light certain observations which may be generalized in spite of the limitations in the study. In our hospital the different types of seizure groups have been categorized

by our expertise neurologists into focal seizures, focal seizures with secondary generalization and generalized seizures. Among focal seizures authors have focal motor seizure (FMS), focal sensory seizures (FSS), and complex partial seizures (CPS).

Among focal seizures with secondary generalization authors have focal motor seizures with secondary generalization (FMSWSG), complex partial seizures with secondary generalization (CPSWSG). Among generalized seizures authors have generalized tonic clonic` seizures (GTCS), myoclonic seizures (MYO), atonic (ATONIC) and absence seizures with secondary generalization. authors have nine different types of seizure groups and for the sake of statistics authors have merged myoclonic, atonic, focal motor, focal sensory and absence with secondary generalization into others. Majority of the participants for the study group were from GTCS which constituted 34% complex partial seizure with secondary generalization were 23%, focal motor seizure with secondary generalization were 17%, complex partial seizure was 14% and others were 12% (Table 2). 56% of epileptic patients had abnormal EEG and the remaining 44% had normal EEG.

For the sake of statistical convenience, the duration of seizure has been grouped into below 5 years. 6-10 years, 11-15 years and 16 years and above. From the study it was found that the most common was 6-10 years which constituted 37%. The second most common was below 5 years which constituted 24%. Seizure frequency was grouped into below 1 per year, 2-5 per year and 5 and above per year. It was found that majority of them had a seizure frequency of 2-5 years which constituted 41% (Table 4).

Patients who continued to take medications regularly were categorized as good compliance and those patients who skipped the medications for 2 to 3 visits were categorized as average compliance and patients who skipped their antiepileptic medications for more than 3 to 4 visits was categorized as having poor compliance. From the study it was found that 59% had good compliance and 26% patients had average compliance and 15% had poor compliance.

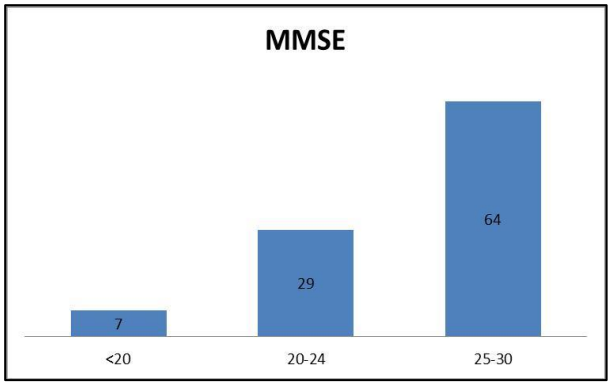

Figure 1: MMSE results.

It was found that 36% of the epileptic patients had cognitive impairment and 64% did not have cognitive impairment. Among the 36% who had cognitive impairment 29% had mild cognitive impairment, 7% had definite cognitive impairment (Figure 1). In the present study, the findings for cognitive impairment were found to be 36% (Table 1 and Figure 1), so present study fairly correlates with the standard literature.[24]

Seizure frequency predicts cognitive dysfunction, the study findings (Table 4) are in agreement with other studies.[25-28] Cognitive impairment may range between 30-44%. On the contrary many previous studies did not mention the prevalence about cognitive dysfunctions.[29,30] There was no statistical significance between complex partial seizure and cognitive decline (Table 3). These findings were in contrast to study done by Cynitha L et al, Harden MD et al, which shows cognitive decline is more in chronic temporal lobe epilepsy compared to other seizure variant.[31] It is obvious from (Table 3) that cognitive decline was seen among atonic, myoclonic, focal sensory, focal motor, absence seizure with secondary generalization. But this finding was in contrast to the studies by Jokeit H et al, and Ebner A et al, which concluded that among temporal lobe epilepsies cognitive decline is more common. [32] While the cross-sectional studies hardly support the idea of an increasing impairment of memory with an increasing duration of epilepsy, there is nevertheless less evidence of significant memory decline over time from longitudinal studies in TLE. [33,34] Likewise, from the (Table 3) it is observed that those who had longer seizure duration had cognitive impairment had low mean cognitive scores and patients who had lesser seizure duration had higher mean scores indicating no cognitive impairment, however the observed difference is not statistically significant. The results also show that cognitive decline is more among epilepsy patients with Abnormal EEG and this observed difference was statistically significant (Table 5). To our best knowledge, this is the first study to find such correlation, so this is considered as a new finding in present study, however this needs further research and future studies.

CONCLUSION

This study was intended to throw some light on cognitive aspects of epileptic patients. Most of the epileptic patients suffer cognitive impairment which goes undetected and untreated so appropriate screening and early detection of cognitive impairment will lead to better treatment outcome of epileptic patients. This study will also create some awareness and help in preventing early onset dementia to some extent.

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