

Evaluation of Cognitive Impairment in Patients with Uncontrolled Epilepsy

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Abstract: The complication of the epileptic patient that is often under-valued and common in the epileptic patients is cognitive impairment particularly when the patients experience poorly controlled seizures. This study was aimed at establishing the degree and trend of cognitive impairment among the uncontrolled patients of epilepsy. It was noted that epilepsy was experienced among 100 patients with a minimum of 2 years experience of epilepsy, and who had frequent attacks yet undergoing sufficient antiepileptic therapy. The cognitive functioning neuropsychological tests and assessments were of memory, attention, executive functioning, and speed of processing. The results revealed that 62 percent of the patients were defined with cognitive impairment of different levels, and the weaknesses were more in the memory and attention domains. There was a significant relationship between such factors as high frequency of seizures, the duration of the epileptic condition, and the polytherapy that covered a combination of antiepileptic drugs ($p < 0.05$). The findings demonstrate the importance of daily cognitive appraisal in epilepsy management, ideal seizure management, and a personal approach to treatment in assisting to address cognitive impairments.

Keywords: Impairments of cognition, uncontrolled epilepsy, treatment with antiepileptic medications, impairment of memory, attention, executive functioning, seizure frequency.

INTRODUCTION

Epilepsy is a persistent neurological condition, which is marked by frequent as well as unprovoked seizures, and it impacts about 50 million individuals around the world. Although the main issue in treating epilepsy is the ability to manage the seizures, cognitive impairment is an easy to find and under-studied complication that can greatly impact the quality of life of patients, their educational achievement, work, and their integration into society. The cognitive impairments of epilepsy can be memory, attention, processing speed, language as well as executive, that occurs in subtle or profound degrees based on factors underlying it [1].

Epilepsy cognitive impairment is multifactorial. Frequent seizures may interfere with neuronal networks and plasticity of synapses and cause structural and functional alterations in the brain. Uncontrolled or prolonged seizures can increase the neuronal damage especially in the hippocampus and temporal lobes which are highly essential in memory and learning. Also, the age of epilepsy onset, the time of the disorder, and the kind of epilepsy (focal and generalized) also contribute to the severity and course of the cognitive impairment [2].

Although necessary to control seizure, antiepileptic drugs (AEDs) may also cause cognitive dysfunction. Polytherapy, high doses, and sedative property medications can have an impact on attention, processing

speed, and memory. Therefore, patients who have epilepsy uncontrolled and have to take multiple AEDs are at more risk of cognitive decline than those with controlled seizures [3]. Cognitive deficits may be further complicated by other factors like comorbid psychiatric conditions, sleep problems and socioeconomic conditions.

Although there have been improvements in diagnosis and treatment, a considerable number of epilepsy patients still face uncontrolled seizures, which means that cognitive assessment is an essential part of the overall treatment of epilepsy. Frequent neurocognitive evaluation is likely to assist clinicians to detect deficits early in the course of treatment, personalize pharmacotherapy, apply cognitive rehabilitation programs, and enhance overall patient outcomes [4].

This research paper will critically review cognitive impairment among epilepsy patients with uncontrolled epilepsy, its prevalence, severity, and most affected domains. It also aims at determining clinical prognostic factors of cognitive impairment, such as the frequency and duration of seizures, the length and kind of AEDs taken. It is assumed that the findings will contribute to the understanding of cognitive effects of uncontrolled epilepsy and direct interventions aimed at maintaining impaired cognitive functioning and maximising seizure control [5].

MATERIALS AND METHODS

Study Design and Setting

The study was a cross-sectional observational research with a duration of six months in the Neurology Department of a tertiary care teaching hospital. The objective of the study was to assess the cognitive impairment among patients with uncontrolled epilepsy and determine the related clinical factors [6].

Study Population

One hundred (100) patients with epilepsy who had at least two years of the disorder with uncontrolled seizures despite sufficient antiepileptic therapy were enrolled. Uncontrolled epilepsy was considered to occur when the individual experiences two or more seizures monthly within the last six months despite proper AED treatment [7].

Inclusion Criteria

- Patients aged 18-60 years.
- Epilepsy diagnosis of 2 years and above.
- Seizures (more than 2 each month) of the AED therapy.
- Readiness to cooperate and sign an informed consent [8].

Exclusion Criteria

- Patients who experience acute symptomatic epilepsy (e.g. as a result of infection, metabolic disturbance).
- Past medical history of significant psychiatric disorder or neurodegenerative disease.
- Far-reaching sensory impairment or language obstacles to cognitive evaluation.
- Clients undergoing sleep drugs that are not part of AED treatment [9].

Data Collection

Ethical Considerations

The Institutional Ethics Committee granted the approval of the study protocol. All the participants provided informed consent in writing [14]. The privacy and confidentiality of patient data were also well observed during the study (Figure 1).

Demographic information (age, gender), clinical history (type of seizure, epilepsy duration, seizure frequency, AED treatment, comorbid conditions), and the results of possible laboratory/neuroimaging were noted [10].

Cognitive Assessment

The cognitive functioning was assessed with the aid of standardized neuropsychological tests [11]:

- Memory: Wechsler Memory Scale(WMS)
- Attention, Concentration: Digit Span Test.
- Executive Process: Trail Making Test (TMT) part A and B.
- Processing Speed: Symbol Digit modalities test (SDMT)

Cognitive impairment was categorized into mild, moderate, and severe according to standardized scoring criteria on each of the tests.

Outcome Measures

- Pattern and prevalence of impaired cognition.
- Correlation between cognitive impairment and the clinical variables e.g. frequency of seizures, duration of epilepsy, type of seizures and the AEDs [12].

Statistical Analysis

The data analysis was done through the SPSS software 25.0. Continuous variables were given in the mean $\pm$ SD and categorical variables in frequencies and percentages. The Chi-square test was used to test the association between categorical variables and independent t-test or ANOVA was used to test the association between continuous variables and cognitive impairment. The level of p-value was considered to be significant (below 0.05) [13].

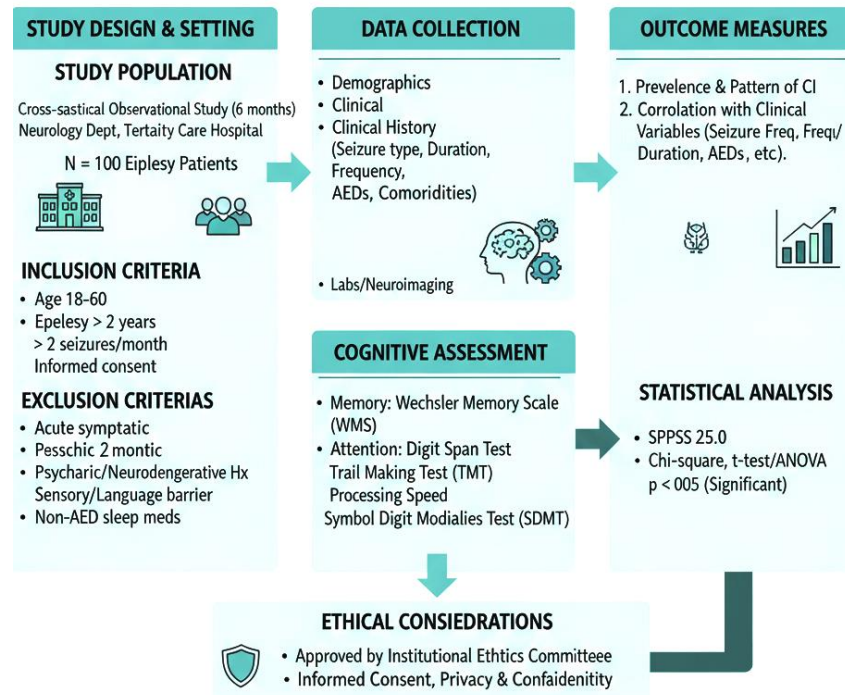


Figure 1: Research Methodology

RESULTS

One hundred patients with uncontrolled epilepsy were recruited to take part in the study. A total of 58 males (58%), and 42 females (42%) participated in the study with a mean age of 34.6 ± 10.2 years. The average years of epilepsy were 8.4 ± 4.7 years and the average number of seizures per month was 3.6 ± 1.2 episodes. Sixty-two percent of patients were on polytherapy (two or more antiepileptic drugs or AEDs) and 38% patients were on monotherapy (Table 1).

Table 1: Demographic and Clinical Characteristics of Study Population (n = 100)

Parameter	Category	Number of Patients (n)	Percentage (%)
Gender	Male	58	58
	Female	42	42
Mean Age (years)	—	34.6 ± 10.2	—
Mean Duration of Epilepsy (years)	—	8.4 ± 4.7	—
Seizure Frequency (episodes/month)	≤ 3	44	44
	> 3	56	56
AED Regimen	Monotherapy	38	38
	Polytherapy (≥ 2 AEDs)	62	62
Seizure Type	Focal with secondary generalization	46	46
	Generalized only	54	54

Prevalence and Pattern of Cognitive impairment

Cognitive impairment was noted in 62 patients (62%) and was categorized in the following way:

- Mild cognitive impairment: 28 (28%) patients.
- Moderate impairment of cognition: 25 patients (25%).
- Severe cognitive impairment: 9 patients (9%) (Table 2)

Table 2: Prevalence and Severity of Cognitive Impairment

Cognitive Impairment Level	Number of Patients (n)	Percentage (%)
None	38	38
Mild	28	28
Moderate	25	25
Severe	9	9

Total Cognitive Impairment	62	62
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Memory and attention areas had been most affected and 48 percent of patients had had a memory deficit and 42 percent had had difficulty with attention. The impairment of executive function was found in 30 per cent of patients and processing speed deficits were found in 25 (Table 3, Figure 2).

Table 3: Cognitive Domains Affected

Cognitive Domain	Number of Patients with Deficit (n)	Percentage (%)
Memory	48	48
Attention and Concentration	42	42
Executive Function	30	30
Processing Speed	25	25

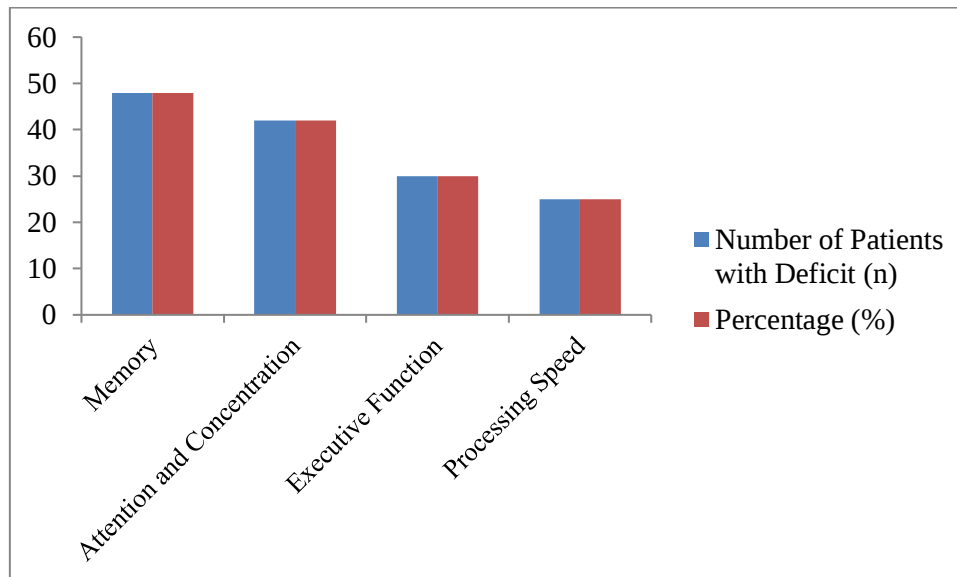


Figure 2: Graphical presentation of Cognitive Domains Affected

Correlation with Clinical Factors

- Frequency of seizures: Patients with the increased seizure frequency (>3/month) were also much more prevalent with cognitive impairment ($p < 0.01$).
- Duration of epilepsy: Patients with the duration of epilepsy >10 years were more prone to cognitive impairments ($p < 0.05$).
- AED regime: Polytherapy was found to have a greater rate of cognitive impairment (72) in comparison to monotherapy (47) (3.00 of less than 0.05).
- Type of seizure: Focal seizures that were affected with secondary generalization were found to lead to more cognitive impairments than generalized seizures in isolation ($p < 0.05$) (Table 4).

Table 4: Association of Clinical Factors with Cognitive Impairment

Clinical Factor	Cognitive Impairment (%)	p-value
Seizure Frequency >3/month	72	<0.01
Epilepsy Duration >10 years	68	<0.05
Polytherapy (≥ 2 AEDs)	72	<0.05
Focal seizures with secondary generalization	70	<0.05

In general, cognitive impairment was observed in 62 per cent of patients with uncontrolled epilepsy. Cognitive domains that were most affected included memory and attention. Cognitive decline was significantly related to higher frequency of seizures, prolonged epilepsy, polytherapy and specific types of seizures. These findings indicate that cognitive impairment in epilepsy is mainly caused by uncontrolled seizures and the complexity of the treatment and therefore the necessity of routine cognitive assessment and optimization of seizure control.

DISCUSSION

The current research tested the cognitive deficiency among uncontrolled epilepsy patients and its relationship with clinical variables. The researchers found out that 62

percent of the study group had cognitive impairments and this is to imply that cognitive impairment is a prevalent and clinical comorbidity in epilepsy particularly in cases where the seizures are not suppressed completely [15]. This occurrence has been regular with the remainder of the literature that puts the rate of cognitive impairment between 50 and 70 percent among patients with chronic or refractory epilepsy.

Memory and attention were the most common and were present in 48 and 42 percent of the patients, respectively. Executive and processing speed was impaired (30 and 25 percent) as well. These findings suggest that the uncontrolled seizures are more influential on high-order mental functions that influence learning, recall and sustained attention which are of utmost importance in the daily lives and quality of life [16]. The above trends of cognitive impairments are not new as the previous studies have already reported it and it is always demonstrated that memory and attention are the most vulnerable in epilepsy.

The increase in frequency of higher seizure significantly correlated with cognitive decrease ($p < 0.01$) which shows that the repetitive epileptiform activity was able to destabilize neuronal networks, and deterioration of cognition processing. Longer period of epilepsy (>10 years) ($p < 0.05$) was also to be linked with the cognitive impairment, which shows that the cumulative effects of prolonged seizure activity on the brain structure and functioning exist [17].

Cognitive impairment was observed to be more likely in two or more antiepileptic drugs (AEDs) polytherapy (72% vs. 47% $p < 0.05$). This finding is consistent with previous ones in which polytherapy, particularly sedative AEDs, is proven to aggravate cognitive impairment due to additive sedative and neurocognitive side effects [18].

Cognition was affected by the type of seizure. The cognitive impairment was found to be greater in patients with focal seizures with secondary generalization compared to those who experience generalized seizure only ($p < 0.05$) which can be likely attributed to the fact that they dealt with the temporal and frontal areas which participate in activities that are vital to memory, attention, and executive functions [19].

These results show the necessity of regular cognitive evaluation of patients with uncontrolled epilepsy. The identification of impaired cognition at an early age may be used to inform therapeutic choices, such as the need to optimally control seizures, use monotherapy where appropriate and cognitive rehabilitation approaches. Moreover, the reduction of polytherapy and the selection of AEDs depending on cognitive side effect profiles could be used to protect cognitive functioning [20].

These study findings are in agreement with the earlier literature that reported that the frequency of seizures,

duration of epilepsy, polytherapy, and type of seizure are significant factors that cause cognitive impairment in epilepsy. Real-life research tends to record higher cognitive impairment than clinical trials because of the presence of patients with refractory or long-term epilepsy and it further validates clinical implications of the study [21].

In sum, the uncontrolled epilepsy has been a major cause of cognitive impairments, especially in memory and attention. Focal seizures, types of seizures, polytherapy, and duration of the disease are major risk factors. Individualized therapy, optimization of seizures, and cognitive monitoring has to be addressed to solve these factors to enhance patient outcomes and quality of life [22].

CONCLUSION

The paper shows that the cognitive impairment among epilepsy patients with uncontrolled epilepsy is of high prevalence as it is present in 62% of the study population. The most frequent areas of influence were memory and attention and the executive function and processing speed were also a bit affected. The clinical variables that were predicted to be of significant importance in more cognitive decline were, higher rate of seizure, longer years of epilepsy, polytherapy use with various antiepileptic drugs, and focal seizures with secondary generalization. These results emphasize the need to do regular cognitive evaluation in management of epilepsy, maximize seizure control and to reduce polytherapy where feasible. Early detection and treatment of cognitive impairment can enhance the quality of life, everyday activities and general treatment results of patients with uncontrolled epilepsy.

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