Magnitude of Cognitive Impairment Among Patients With Epilepsy at Health Institutions in Gurage Zone, Ethiopia

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Abstract

Introduction: Epilepsy is a widespread neurological disorder characterized by recurrent unprovoked seizures; it contributes to 1% of the global burden of diseases and can end in cognitive impairment.
Objective: To assess the magnitude and associated factors of cognitive impairment among patients with epilepsy.
Method: The study utilized an institution-based cross-sectional study design. All patients with epilepsy whose ages were above 18 years were the source population. The authors performed bivariate and multivariate logistic regression analyses. Finally, variables with a p-value <.05 were significantly associated.
Result: The magnitude of cognitive impairment is 25.6%. Having no family history of epilepsy (AOR=0.12; 95% CI [0.02, 0.61]), polytherapy (AOR=5.14; 95% CI [1.12, 23.62]), and medication-related complaints (AOR=8.24; 95% CI [1.87, 36.38]) were strongly associated with cognitive impairment.
Conclusion: Significant numbers of patients were positive for cognitive impairment. Family history, polytherapy, and medication-related complaints were associated factors.

Introduction

A seizure is an abnormal and excessive electrical discharge that can be classified as focal onset if excessive firing is limited to a small area of the brain; otherwise, it is called a generalized onset (Dekker, 2002). Epilepsy is one of the most widespread neurological disorders characterized by recurrent unprovoked seizures (World Health Organization, 2010). One can classify a seizure as symptomatic or unknown based on whether it has an identified cause (Dekker, 2002). Current estimates suggest that it contributes to 1% of the global burden of diseases (World Health Organization, 2005). Globally, seizure affects more than 60 million people (Ngugi et al., 2009). Worldwide, there are 33 million affected children; of these, 85% are in under-resourced countries, where the prevalence is two to three times higher than in industrialized countries (Newton & Garcia, n.d.; Preux & Druet-Cabanac, 2005). Eighty percent of patients with seizures in sub-Saharan countries experience the first onset of seizures below 18 years of age

(Duggan, 2010, Mang'ala et al., 2008; Preux & Druet-Cabanac, 2005). It results from repeated seizure episodes and anti-epileptic drug side effects (Kupfer, et al., 2008; Li et al., 2022). Cognitive impairment can be a general or specific cognitive decline, such as general mental slowness, memory impairment, and attention deficits (Moorthy et al., 2018). Various clinical factors contribute to cognitive impairment, including the age of onset, seizure type and severity, anti-epileptic drugs, and other factors (Alden Kamp, 2006; Jokeit & Ebner, 2002). If the seizure starts early, the outcome also will be poor. The degree and duration of illness are also known predictors of cognitive

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challenges (Iqbal et al., 2006). In addition to chronicity and highly demanding features, the cognitive outcome of seizures affects many patients. Medication adherence will be low if the patients experience cognitive impairment, particularly memory (Gurumurthy et al., 2017). Primarily, seizure control depends on treatment adherence. If medication adherence is poor, the possible treatment outcome will be inadequate (Zewudie et al., 2020). Despite 61% to 72.8%, the African population earns less than 1.00 US$ per day; the annual cost of seizure control with phenobarbital and phenytoin at 100 mg per day varies from US$1.00 to 150.00, and US$2.00 to 69.00, respectively. Therefore, cognitive impairment hinders development by increasing the annual cost of seizure control (World Health Organization, 2004). Cognitive impairment is problematic and needs a solution in our country. However, to decrease its effect, due attention has not been given. Knowing the magnitude and associated factors of cognitive impairment is helpful in the problem. Even though regular neurological assessment of the patient is crucial to identify the degree of cognitive impairment, there is no such practice in the study area (Zhu et al., 2022). It is because, in the study area, there is no neurologist and EEG; thus, the psychiatry nurses make the diagnosis clinically. Therefore, the level of cognitive functioning of the patients is unknown. Though assessing the degree of cognitive impairment is necessary to help the patients. It is worthwhile to research to identify the level of cognitive functioning. There is one study conducted at Blackline Hospital. However, participants of the previous study had very different socio-demographic statuses (Gugessa et al., 2011). Thus, it was reasonable to conduct this study in this area. Finally, the finding will be an input to enhance the service and improve the quality of life and also will be a reference for the researchers. Therefore, the studies aimed to assess the magnitude and associated factors of cognitive impairment among patients with epilepsy who attended the follow-up at Gurage Zone hospitals in Ethiopia.

Literature Review

Prevalence of Cognitive Impairment Among Patients With Epilepsy

The studies conducted in Indonesia about cognitive impairment among patients with epilepsy indicate the prevalence of cognitive impairment varies from 17.6% to 83.9% (Lestari et al., 2020; Zhu et al., 2022). A comparative study in Pakistan indicates that Epileptic patients have more cognitive impairment than psychogenic non-epileptic patients (Kausar et al., 2021). A similar study in Pakistan also indicated that 39.5% of patients with epilepsy had experienced cognitive impairment secondary to epilepsy (Malik et al., 2019).

The cognitive function of patients with epilepsy is lower than that of normal individuals. A finding in Brazil witnessed that 38% of patients with epilepsy experienced a cognitive decline (Tedrus et al., 2020). Research conducted at a neurologic clinic in Malaysia confirmed that 37.2% of patients with epilepsy had experienced cognitive impairment (Beh et al., 2020). A study conducted in Tunisia to evaluate the frequency of cognitive impairment among patients with temporal lobe epilepsy witnessed that more than half of the patients experienced cognitive impairment (Nouha et al., 2018).

A study conducted in Burkina Faso to describe cognitive disorders in patients with epilepsy attending neurology consultations revealed 25.5% of patients had cognitive impairment (Dabilgou et al., 2019). Also, a study done on the prevalence of cognitive-adverse outcomes in epileptic outpatients showed that 17.26% of the patients experienced cognitive impairment (Merkena, 2016).

Associated Factors

Cognitive impairment among patients with epilepsy is multifactorial. Studies identified many factors: socio-demographic variables, the seizure type, anti-epileptic drugs, age of onset, seizure frequency, and duration of seizure disorder.

Age is one of the factors which increases the risk of cognitive impairment among those with epilepsy; as the age increase, epilepsy-related cognitive impairments increase (Beh et al., 2020; Wang et al., 2019; Malik et al., 2019; Masoudian et al., 2020).

Educational level is another factor that affects the occurrence of cognitive impairment among epileptic patients; studies identified cognitive impairment is inversely associated with education level (Beh et al., 2020; Harahap et al., 2022; Wang et al., 2019).

The risk of cognitive impairment amplified with poly drugs. Combining drugs that have the similar effect has high degree of neurotoxic effect, it becomes the basis for cognitive decline in epilepsy patient with Polydrug. Studies indicate that polydrug prescription affects cognitive functioning negatively (Beh et al., 2020; Lestari et al., 2020; Novak et al., 2022).

Because some epilepsy syndromes are genetically determined, maternal breathing problem during seizure attack, and teratogenic effect of anti-epileptic drugs, a family history of epilepsy increase the risk of cognitive impairment; studies identified that having a family history of epilepsy increase the risk of developing cognitive impairment among patients with epilepsy (Lin et al., 2021).

Methods and Materials

Study Area and Study Period

The study was conducted at hospitals in the Gurage zone, Southern Nations, Nationalities, and People Region, Ethiopia, from 12 September to 28 February 2020/2021.

Study Design

An institution-based cross-sectional study was utilized.

Population. **Source population**: All patients with epilepsy whose ages were > 18 and who attended the follow-up at the Gurage Zone hospitals.

Study population: All patients with epilepsy whose ages were > 18 and who attended the follow-up at the Gurage Zone hospitals during the study period.

Research Question

What is the prevalence of cognitive impairment among patients with epilepsy who attended?

What are the associated factors for cognitive impairment?

Sample Size Determination and Sampling Technique. **Sample size determination:** The authors used a single population proportion formula and the computed sample size at a *p*-value of 17.26% (Varkevisser et al., 2003), a margin of error of 0.04, and a confidence interval at (Zα/2) of 95%. n = Z2 p (1-p) / w2 (Dr. D. William Molloy & Dr. Roger Clarnette, n.d.).

N= (1.96)2×0.1726×(1−0.1726)×(0.04)2=343.

Since the total population is <10,000, the authors adjusted the sample size using the correction formula: N= source population

n= sampled population n / (1+ n/N) = 343 / (1+ 343/1980) = 292 (Merkena, 2016).

Sampling technique: The authors utilized a systematic random sampling technique.

Inclusion and Exclusion Criteria. **Inclusion criteria:** All patients with epilepsy whose ages were> 18 were included in the study.

Exclusion criteria: All patients with pre-existing neuro-cognitive disorders and intellectual disabilities were excluded from the study.

Data Collection Procedure. **Data collection instrument**: The authors used a Mini-Mental State Examination tool to assess cognitive impairment. It is the most widely used, and people can administer it in a few minutes. The Mini-Mental State Exam scale assesses Language, Attention, Execution Memory, and apraxia. Each item has 0 or 1 value, and the total score was obtained by adding all points; if the total score is below 24, generally considered impaired (Varkevisser et al., 2003).

Data collection procedure: To collect the data, the authors divided the sample size of each hospital as follows:

n1= sample size for each hospital; N1= total number of patients who attended the follow-up at each hospital; N= total number of patients who attended at both hospitals. The sample sizes for Atata hospital and Butajira hospital

were (N1n/N= 292×480/1980=71) and (N1n/N= 292×1500/1980=221), respectively. Since the actual appointment was unknown, it was impossible to find a sampling frame. So, the authors used a systematic random sampling technique. Before the authors used systematic random sampling, the authors calculated the sampling interval (*k*) by dividing the total population by the sampled population of each hospital respectively (Degu & Tessema, 2005). Thus, *K* was 7. Consequently, the study included every 7th patient from Butajira and Atat hospitals.

Data Quality Assurance

The authors performed a pre-test on 5% of the study subjects in none selected hospitals. Before entry, the team reviewed and checked for completeness. The authors cleaned the data by running a simple frequency. The authors checked the inconsistent data by comparing it to the hard copy of the questionnaire.

Data Processing and Analysis

Since the data were categorical, we used binary logistic regression. The authors performed descriptive and bivariate analyses using a statistical package for social science (SPSS) version 21. The authors transferred a variable with a *p*-value below 0.25 in the bivariate analysis with multivariate logistic regression. The authors checked the goodness of fit by Hosmer and Lemeshow test; the data fitted to the model (*p*>0.08). Similarly, the authors test the collinearity by calculating VIF. The VIF values of variables were nearly 1. Therefore, there was no collinearity. Finally, the authors declared independently associated variables at a *p*-value of <.05. The authors described the degree of association using odds ratios and a 95% confidence level (2017).

Operational definition: The authors declared cognitive impairment at the cutoff point <24 of mini mental state examination (MMSE).

Results

The Socio-Demographic Characteristics of the Participants

Of the total 292 study subjects, the authors involved 285 (97.6%) in the study. The response rate was 97.6%. Of the study subjects, the majority, 206 (72.3%), were males. Concerning the family history of epilepsy, of the total study subjects, 233 (81.8%) had no family history of epilepsy.

Seizures and treatment-related characteristics of participants: Of the participants, nearly 273 (95.8%) have experienced a generalized tonic-clonic seizure. Preponderance, 190 (66.7%) of the patients had experienced the seizure onset between 10 and 20 years of age. The study also

identified whether patients had medication-related complaints; 261 (91.6%) had complaints about the anti-epileptic drug.

Cognitive Impairment

In this study, the mean value of the mini-mental state examination score was 25.08, with minimum and maximum scores of 8 and 30, respectively. Similarly, of the total, 73 (25.6%) scored below 24. The following chart shows the mini-mental state examination score of the participants (Figure 1).

Associated Factors

The authors rigorously analyzed the factors included in this study to identify whether there are associations with the outcome variable. Thus, a family history of epilepsy, polytherapy, and medication-related complaints was significantly associated with cognitive impairment. Accordingly, patients with a family history of epilepsy had 0.12 times less chance of developing cognitive impairment than those with a family history (AOR=0.12; 95% CI [0.02, 0.61]). The patients who take polydrugs were 5.4 times more likely to develop cognitive impairment than those who take a single drug (AOR=5.4; 95% CI [1.12, 23.62]). Finally, patients with medication-related complaints were 8.24 times more likely to have cognitive impairment than those without (AOR=8.24; 95% CI [1.87, 36.38]). The following table shows the binary and multivariable logistic regression of cognitive impairment (Tables 1 to 3).

Discussion

This study identified the magnitude of cognitive impairment and associated factors among patients with epilepsy and those who attended the follow-up at Gurage zone hospitals. Of the study subjects, 175 (95.1%) had been experiencing a generalized tonic-clonic seizure. The high prevalence of generalized tonic-clonic seizures might be because of diagnostic modalities; since there was no EEG in the current study area. Clinicians in this study area were diagnosing the patients based on symptomatology. Therefore, they might face the challenge of identifying each subtype of epileptic seizure and their respective treatments. It may contribute to experiencing long-standing epilepsy. The overall magnitude of cognitive impairment was 22.8%, with the mean and the lowest score of 25.79 and 8, respectively. It is lower than the study conducted in Pakistan and India which revealed that the prevalence was 36–39.5% (Malik et al., 2019; Malik et al., n.d.). The discrepancy might be because some participants of the previous studies had comorbid psychiatric illnesses like anxiety and depression that might worsen their cognitive impairment (Iqbal et al., 2006). On the other side, this result is a little higher than a finding from Addis Ababa, Ethiopia, indicating that cognitive impairment was 17.26% (Merkena, 2016). As far as the mini-mental state examination tool is affected by educational status, the discrepancy might be due to educational status differences. All participants of Addis Ababa's study were literate. Whereas 17.4% of the current study's participants were illiterate; likewise, when we consider tertiary education level, it was 20.8% in the previous study, whereas it was 13.6% in the current study. Hence, all of these might cause a difference in the magnitude of cognitive impairment between the two studies. Therefore, as patients' educational status increased, the mean score of MMSE also raise. Hence, the majority of the participants in the current study were of low education status. It indicates either they may not attend their education or discontinue because of the cognition-demanding nature of education.
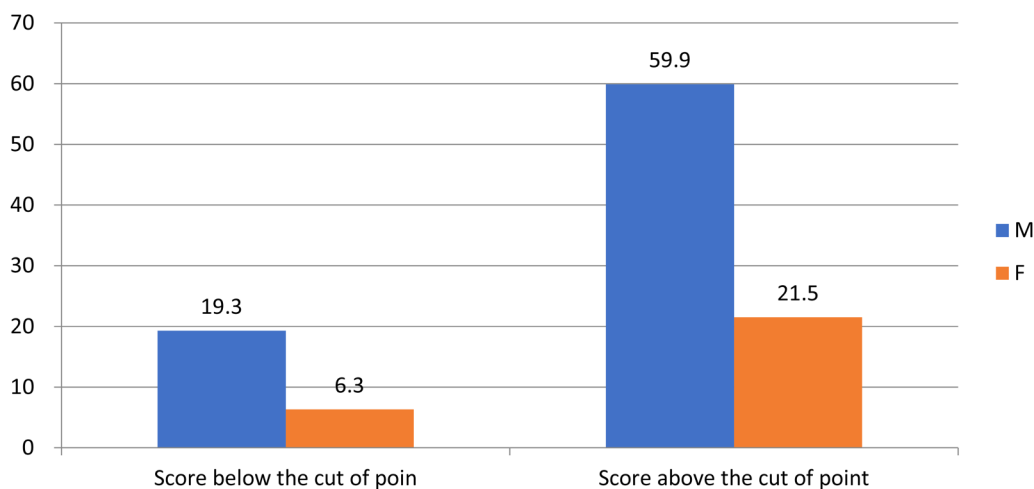
Figure 1. Mini-mental state examination score of the patients with epilepsy who attended the outpatient clinic in Gurage Zone Hospital, Gurage, Ethiopia, 2020/2021.

Table 1. Socio-demographic Characteristics of Participants Who Attended the Outpatient Clinic in Gurage zone hospitals, 2020/2021 (n=184).

S. N	Variables	Category	Frequency (n)	Percent (%)	Mean MMSE (SD)
1	Age	18–20	46	16.1	26.80± 4.81
		21–29	122	42.8	24.62± 6.44
		30–39	61	21.5	26.33± 3.29
		40–49	46	16.1	22.80± 9.30
		50–59	10	3.5	25.70± 1.77
2	Religion	Orthodox	77	27.0	26.47± 4.58
		Muslim	178	62.5	24.31± 6.53
		Protestant	27	9.5	25.70± 7.98
		Catholic	3	1.0	30.00± 0.00
3	Educational status	Illiterate	48	17.2	24.85± 4.82
		Grade 1–8	121	43.4	25.03± 5.12
		Grade 9–12	75	26.8	26.04± 5.77
		College and above	35	12.6	27.83± 3.07
4	Occupation	No occupation	16	5.6	21.75± 7.06
		Government employer	43	15.1	28.07± 3.99
		Farmer	89	31.2	25.04± 6.24
		Merchant	7	2.5	26.00± 5.48
		Student	60	21.1	23.73± 7,05
		Housewife	30	10.5	24.13± 8.50
		Day laborer	40	14	25.89± 2.99
5	Marital status	Single	162	56.9	25.01± 6.17
		Married	85	29.8	24.64± 7.18
		Divorced	28	9.8	26.43± 4.20
		Widowed	10	3.5	26.20± 3.5
6	Ethnicity	Gurage	191	67.0	24.65± 6.51
		Amhara	29	10.2	29.03± 1.32
		Oromo	16	5.6	22.94± 4.68
		Silte	35	12.3	26.46± 5.11
		Others	14	4.9	21.5± 8.64

Nearly one in four of the current participants are still experiencing an epileptic seizure attack daily up to once in six months; of the participants, the majority have suffered from the disease for more than ten years. The chronicity of the seizure can be due to not seeking medical treatment early or not getting the appropriate treatments for the problem. Thus, both cases might contribute to the declining MMSE score of the patient below the cut point. A family history of epilepsy was a significantly associated factor in this study. Therefore, having no family history of epilepsy 0.12 times ($p< .011$) decreases the chance of developing cognitive impairment; this is in line with a study conducted in various parts of the world (Kumar & Vatsala 2019; Titze et al., 2008). It might be because maternal exposure to anti-epileptic drugs during pregnancy increases the risk of cognitive impairment for their siblings who are patients with epilepsy (Powell et al., 2015). A family history of epilepsy contributed to anti-epileptic drug resistance, which resulted in cognitive impairment (Moorthy et al., 2018). The number of anti-epileptic drugs the patient has been taking is significantly associated with cognitive impairment 5.14 times ($p< .035$).

Therefore, taking more than a drug may increase the risk of cognitive impairment (Lestari et al., 2020; Moorthy et al., 2018; Novak et al., 2022; Wang et al., 2019). In addition to the disease process of epilepsy, cognitive impairment could result from anti-epileptic drug side effects; if the patient takes more than one medication, the synergetic anti-epileptic drug side effect might impair cognitive function. In addition, cognitive impairment might be because of uncontrolled seizures that might be resulted from the unaffordability of Polytherapy (Zewudie et al., 2020). This study indicates experiencing discomfort towards the medication was associated ($p< .005$) with cognitive impairment. Cognitive impairment might occur because of poor anti-epileptic drug adherence that might be secondary to pill burden (Malik et al., 2019). Limitation MMSE is sensitive to educational status. The majority of participants attended low levels of education. It might inflate cognitive impairment; since MMSE is a screening tool, it can't diagnose the existing intellectual disorder. There is no EEG service, and the clinicians have diagnosed the patient based on signs and symptoms that may include a non-epileptic seizure.

Table 2. Seizure and Treatment-related Characteristics of Participants Who Attended the Outpatient Clinic in Gurage zone hospitals, 2020/2021 (n=285).

S.N	Variables	Category	Frequency (n)	Percentage (%)	Mean MMSE(SD)
1.	Types of seizure	Generalized tonic-clonic seizure	273	95.8	25.00 ± 6.35
		Focal seizures with impaired awareness	12	4.2	27.00 ± 3.33
2.	Age of seizure onset	<10	64	22.5	23.39 ± 7.44
		10–20	190	66.7	25.36 ± 5.51
		21–45	31	10.9	26.90 ± 7.32
		Mean	15.36 ± 7.17		
3.	Duration in years	<10	75	26.3	28.01 ± 3.83
		11–20	37	13.0	23.03 ± 8.01
		21–30	106	37.2	25.72 ± 5.29
		>30	67	23.5	21.94 ± 7.07
		Mean	12.99 ± 9.06		
4.	Seizure frequency	Daily to every other day	30	10.5	22.87 ± 7.78
		Weekly to every other week	16	5.6	20.75 ± 6.55
		Once in three to four weeks	33	11.6	20.64 ± 6.81
		Once in the past 1–6 months	83	29.1	25.44 ± 4.94
		6–11 months ago	39	13.7	27.79 ± 2.18
		1–4 years ago	25	8.8	28.16 ± 1.70
		>= 5years ago	45	15.8	26.97 ± 6.42
		No seizure in the last six month	14	4.9	24.00 ± 10.29
5.	Monotherapy	Phenytoin	4	1.8	28.10 ± 1.00
		Phenobarbital	19	8.3	26.47 ± 6.95
		Valproate	205	89.9	24.69 ± 6.02
6.	Polydrug	PHN+PHB	17	29.8	29.76 ± 0.44
		PHN+CBZ	18	31.6	22.22 ± 9.23
		PHN+VAL	4	7.0	22.00 ± 14.69
		PHB+CBZ	14	24.6	26.07 ± 1.89
		PHB+VAL	4	7.0	29.00 ± 0.00
7.	Frequency of taking medication	Once-daily	188	66.0	25.72 ± 5.88
		Twice daily	97	34.0	25.08 ± 6.26

Table 3. Binary and Multivariate Logistic Regression of Cognitive Impairment Among Patients With Epilepsy Who Attended the Outpatient Clinic in Gurage zone hospital, 2020/2021.

		Cognitive impairment				
Variables	Category	Yes (n/%)	No (n/%)	COR (95% CI)	AOR (95% CI)	*p*-value
Educational status	Illiterate	10(10.8)	22(24.2)	.191 (.04, .97)	.40(.049, 3.20)	.384
	Grade 1–8	22(12)	55(29.9)	.217 (.05, 1.00)	.27(.05, 1.61)	.150
	Grade 9-12	8(4.3)	42(22.8)	1.325(.09, 2.33)	1.15(.17, 7.66)	.882
	College & above	2(1.1)	23(12.5)	1.00	1.00	
Family history of epilepsy	Yes	31(16.9)	2(1.1)	1.00	1.00	
	No	111(60.3)	40(21.7)	.521(.24, 1.13)	.12(.02,.610)	.011*
Monotherapy	Yes	39(21.2)	108(58.7)	1.00		
	No	3(1.6)	34(18.5)	4.093(1.19, 14.09)	5.14(1.12, 23.62	.035*
Comfortable with medication	No	8(4.3)	8(4.3)	3.941 (1.38, 11.26)	8.24(1.87, 36.38)	.005*
	Yes	34(18.6)	134(72.8)	1.00	1.00	

*Significantly associated variables.

Strength and Limitation

Strength: The study used a margin error of 00.4 so that it can increase the precision.

Limitations: Mini-mental state examination tool is affected by education level, which causes a false positive result.

Implication for Practice

The finding gives an insight to Zone health department officials so that they can organize training. By doing so, the system will enhance the quality of the service: patients' treatment outcomes will be good, and the occurrence of cognitive impairment will decrease. Also, it can be an alarm for health professionals to be cautious when they order anti-epileptic drugs: and it can also make the professionals responsive to any anti-epileptic medication-related complaints.

Conclusion

Although MMSE is a screening tool, it identified a significant number of study participants who were positive for cognitive impairment. Medication-related complaints, a family history of epilepsy, and taking polydrugs were strongly associated with cognitive impairment.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical Consideration

The research team obtained ethical approval from Wolkite University, the college of medicine, health science research, and the community service coordinator; the health department wrote a formal letter to the concerned body. The data collectors explained the objective to responders, and the participation of responders was strictly voluntary, and patients gave informed consent. We assured the respect, dignity, and freedom of responders.

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References

Aldenkamp, A. P. (2006). Cognitive impairment in epilepsy: State of affairs and clinical relevance. *Seizure-European Journal of Epilepsy*, *15*(4), 219–220.

Beh, H.-C., Tan, H.-J., Hod, R., Khoo, C.-S., & Mohamad, K. (2020). Prevalence and factors influencing visual memory dysfunction among epilepsy patients—a single-center study. *Neurology India*, *68*(3), 581–585. https://doi.org/10.4103/0028-3886.289011

Dabilgou, A. A., Dravé, A., Adeline, M. J., Kyelem, K. A. N., Napon, C., Millogo, A., & Kaboré, J. (2019). Cognitive disorders in patients with epilepsy attending neurology outpatient clinics. *A Multicenter Prospective Cross-Sectional Study from Burkina Faso*, *3*(1), 013–017.

Degu, G., & Tessema, F. (2005). *Biostatistics lecture notes for Health Science Students*. Ethiopia Public Health Training Initiative.

Dekker, P. A. (2002). *A manual for Medical and Clinical Officers in Africa*. World Health Organization.

Duggan, M. B. (2010). Epilepsy in rural Ugandan children: Seizure pattern, age of onset and associated findings. *African Health Sciences*, *10*(3), 218–225.

Gugssa, S. A., Davey, G., Ejigu, A. A., Metaferia, G. Z., Medhin, G., & Kelkile, T. S. (2011). Population norms for the mini-mental state examination. *Ethiopian Medical Journal*, *49*(3), 239–247.

Gurumurthy, R., Chanda, K., & Sarma, G. R. K. (2017). An evaluation of factors affecting adherence to anti-epileptic drugs in patients with epilepsy: A cross-sectional study. *Singapore Medical Journal*, *58*(2), 98–102. https://doi.org/10.11622/smedj.2016022

Harahap, H. S., Rizki, M., & Irawati, D. (2022). Factors associated with global cognitive impairment in epilepsy patients: A cross-sectional study in Mataram, Indonesia. *Medical Journal of Indonesia*, *31*(3), 155–159. https://doi.org/10.13181/mji.oa.226118

Iqbal, K. M., Rambe, A. S., & Sjahrir, H. (2006). Correlation between anxiety and depression symptoms with seizure severity in epilepsy patients at neurology department Haji Adam Malik hospital Medan, North Sumatra, Indonesia. *Bersama Kita Maju*, *87*(2).

Jokeit, H., & Ebner, A. (2002). Effects of chronic epilepsy on intellectual functions. *Progress in Brain Research*, *135*(455–63).

Kausar, N., Qurban, H., & Bibi, B. (2021). A comparative study to investigate the level of cognitive impairment among epileptic and psychogenic non-epileptic patients. *Journal of the Pakistan Medical Association*, *71*, 420–423. https://doi.org/10.47391/JPMA.283

Kumar, V. J., & Vatsala, M. (2019). Cross sectional study to determine the cognitive impairments among epilepsy patients. *International Journal of Research in Medical Sciences*, *7*(5), 1465–1471. https://doi.org/10.18203/2320-6012.ijrms20191463

Kupfer, D. J., Horner, M. S., Brent, D. A., Lewis, D. A., Reynolds, C. F., Thase, M. E., Travis, M. J., Semple, D., Smyth, R., Burns, J., Darjee, R., & McIntosh, A. (2008). *Oxford American Handbook of Psychiatry* (1st ed.).

Lestari, N. D., Rizkidawati, R., Shafira, C. P., Suherman, S., & Mutiawati, E. (2020). Factors affecting the mini-mental state examination (MMSE) score in the epilepsy patients in Aceh, Indonesia. *Bali Medical Journal*, *9*(1), 185–188.

Li, L., Lu, J., Xu, Y., & Zhao, Y. (2022). Changes in Pre- and post-surgery for drug-resistant epilepsy: Cognition and sleep. *BioMed Research International*, *2022*, 1–7. https://doi.org/10.1155/2022/9971780

Lin, F., Han, J., Xue, T., Lin, J., Chen, S., Zhu, C., Lin, H., Chen, X., Lin, W., & Huang, H. (2021). Predicting cognitive impairment in outpatients with epilepsy using machine learning techniques. *Scientific Reports*, *11*, https://doi.org/10.1038/s41598-021-99506-3

Malik, M., Hussain, A., Malik, S., & Hashmi, A. (n.d.). Cognition and memory impairment among patients of epilepsy in Pakistan-the role of conventional and newer anti-epileptics. *Clinical Research*, *6*.

Malik, M., Hussain, A., Malik, S., & Hashmi, A. (2019). Cognition and memory impairment among patients of epilepsy in Pakistan-The role of conventional and newer anti-epileptics. *International Journal of Scientific Research, 8*(1). https://doi.org/10.19080/JPCR.2019.08.555726

Mangala-Odera, V., White, S., Meehan, R., Otieno, G. O., Njuguna, P., & Mturi, N. (2008). Prevalence, incidence and risk factors of epilepsy in older children in rural Kenya. *Seizure*, *17*(5), 396–404.

Masoudian, N., Moradpour, M., Samaei, A., Ehsani, F., & Ziari, A. (2020). Assessment of cognitive functions and related risk factors in Iranian patients with generalized epilepsy compared to non-epileptic neurological disorders. *Current Journal of Neurology*, *19*(4), 167–172.

Merkena, M. D. (2016). Prevalence of cognitive-adverse outcomes in epileptic outpatients. *Journal of Neurology & Stroke*, *4*(5), 00155.

Moorthy, M. P., Srinivasan, A. V., & Bhanu, K. (2018). Cognitive Impairment In Epilepsy. *7*(4).

Newton, C. R., & Garcia, H. H. (n.d.). Epilepsy in poor regions of the world. *Epilepsia*, *380*(–), 1193–1201.

Ngugi, A. K., Bottomly, C., Kleinschmidt, S. J., & Newton, C. R. (2009). Estimation of the burden of active and lifetime epilepsy: A meta-analytic approach. *Epilepsia*, *51*, 883–890.

Nouha, F., Sawsan, D., Salma, S., Olfa, H., Hanen, H. K., Mariem, D., & Chokri, M. (2018). Cognitive impairment in patients with temporal lobe epilepsy. *Journal of Neuropsychiatry*, *2*(5). https://doi.org/10.21767/2471-8548.10009

Novak, A., Vizjak, K., & Rakusa, M. (2022). Cognitive impairment in people with epilepsy. *Journal of Clinical Medicine*, *11*(1), 267. https://doi.org/10.3390/jcm11010267

Powell, K., Walker, R. W., Rogathe, J., Gray, W. K., Hunter, E., Newton, C. R., & Burton, K. (2015). Cognition and behavior in a prevalent cohort of children with epilepsy in rural northern Tanzania: A three-year follow-up study. *Epilepsy & Behavior*, *51*(–), 117–123. https://doi.org/10.1016/j.yebeh.2015.06.034

Preux, P. M., & Druet-Cabanac, M. (2005). Epidemiology and etiology of epilepsy in sub-Saharan Africa. *The Lancet Neurology*, *4*, 21–31.

Tedrus, G. M. A. S., Passos, M. L. G. A., Vargas, L. M., & Menezes, L. E. F. J. (2020). Cognition and epilepsy cognitive screening test. *Dementia & Neuropsychologia*, *2*(14), 186–193.

Titze, K., Koch, S., Helge, H., Lehmkuhl, U., Rauh, H., & Steinhausen, H.-C. (2008). Prenatal and family risks of children born to mothers with epilepsy: Effects on cognitive development. *Developmental Medicine & Child Neurology*, *50*, 117–122.

Varkevisser, C., Pathmanathan, I., & Brownlee, A. (2003). *Designing and Conducting Health Systems Research Projects*. KIT.

Wang, L., Chen, S., Liu, C., Lin, W., & Huang, H. (2019). Factors for cognitive impairment in adult epileptic patients. *Brain and Behavior*, *10*, 1475. https://doi.org/10.1002/brb3.1475

William Molloy, D., & Clarnette, R. (n.d.). *A standardized mini-mental state examination*.

World Health Organisation. (2005). *Atlas: Epilepsy Care in the World*. WHO.

World Health Organization. (2004). *The Global Campaign Against Epilepsy Out of the Shadows*.

World Health Organization (2010). *MhGAP Intervention Guide for mental, neurological and substance use disorders in non-specialized health settings (Vol. 1–1)*.

Zewudie, A., Mamo, Y., Feyissa, D., Yimam, M., Mekonen, G., & Abdela, A. (2020). Epilepsy treatment outcome and its predictors among ambulatory patients with epilepsy at Mizan-Tepi University Teaching Hospital, Southwest Ethiopia. *Neurology Research International*, *2020*, 1–8. https://doi.org/10.1155/2020/8109858

Zhu, Q., Zhang, J., Wang, X., & Fang, Y. (2022). Influencing factors for cognitive impairment in patients with dorsolateral frontal lobe epilepsy. *Neurology Asia*, *27*(2), 301–308. https://doi.org/10.54029/2022crv