IAA Journal of Biological Sciences 7(1):21-32, 2021. ISSN: 2636-7254

The prevalence of cognitive impairment in adult patients with epilepsy attending UBTH and FMC Owerri

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ABSTRACT

Epilepsy is a major global public health issue especially in developing countries like Nigeria. Its prevalence in Nigeria varies from 15 to 37 per 1000. Cognitive dysfunction has been noted in patients with epilepsy and this has been attributed to some risk factors including duration of epilepsy before treatment, frequency of seizures before treatment and type of antiepileptic drugs. There is limited evidence regarding the risk factors for cognitive dysfunction among patients with epilepsy in Nigeria. The aim of this research was to assess the prevalence of cognitive impairment in adult patients with epilepsy attending UBTH and FMC Owerri. A hospital-based cross-sectional case-control study of consecutively recruited 100 adult patients with 50 controls from UBTH and 50 patients with 25 controls from FMC Owerri. The patients were clinically diagnosed with epilepsy with or without Electroencephalogram (EEG) and matched for age, sex and level of education (150 cases and 75 controls in total). A pilot study was done to adapt the original Montreal Cognitive Assessment (MOCA) to the local context and a cutoff of 22 was determined. The participants were then assessed using "The Iron Psyche" (FEPSY) and the adapted MOCA tools. Statistical analysis was done using SPSS version 25. Risk factors of cognitive dysfunction were determined using logistic regression analysis. A p-value of <0.05 and 95% confidence interval were set for level of significance. The mean age of the participants was 25 years (±SD 5.2) for cases and 26 years (±SD 6.4) for controls, with male to female ratio of 1.6:1. Among the study participants, 80% of the cases and 74.7% of the controls had secondary level of education. In concluson a prevalence of 20.7% was observed for cognitive dysfunction using MOCA.

Keywords: Prevalence, cognitive impairment, epilepsy.

INTRODUCTION

Cognition comes from the Latin root *cognoscere*, which means "to know". It usually refers to everything that is related to knowledge. It can also be referred to as the accumulation of information acquired through learning or experience [1]. The most accepted definition of cognition is the ability to process information though perception, knowledge acquired through experience, and subjective characteristics that allow the integration all of the information, to evaluate and interpret the world [2,3]. Cognition is the ability to assimilate and process the information received from different sources (perception, experience, beliefs) to convert them into knowledge [4]. Cognition includes different cognitive processes, like learning, attention, memory, language, reasoning, decision making. Cognitive processes are the procedures used to incorporate new knowledge and make decisions based on the knowledge[5,6,7]. Different cognitive functions play a role in these processes: perception, attention memory and reasoning. Each of these cognitive functions works together to integrate the new knowledge and create an interpretation of the world [8].

In epilepsy, some of these cognitive processes are affected thereby making the patients to manifest with some forms of cognitive deficits [9]. Several relationships have been obtained between cognitive impairment and epilepsy-related or treatment-related factors [10]. One of these factors is treatment-related: the central cognitive

side effects of the antiepileptic drugs (AEDs) [11]. The second and third factors are disease-related factors; the effect of the seizures and underlying epileptiform discharges in the brain and the localization of the epileptogenic focus in specific areas of the brain. Although most cognitive problems have a multifactorial origin and often several factors combined are responsible for the cognitive problem, an attempt has been made to isolate one factor; the effect of seizures and epileptiform EEG discharges on cognitive function [12]. There are some risk factors that have been associated with cognitive deterioration in epilepsy. These include;

- Duration of epilepsy: Longer duration of epilepsy has been reported to be associated with greater cognitive impairment. The negative impact of duration may be in part due to the cumulative impact of seizures, but also to other factors including antiepileptic drug (AED) treatment and pathologic interictal brain activity [13].
- Age of onset of seizure: An early age of onset is a risk factor for cognitive decline, as brains are less able to develop a functional reserve capacity to cope with subsequent loss. Advancing age, conversely, has been proposed as increasing the risk of cognitive decline, because having epilepsy accelerates the cognitive aging process[14].
- Duration between the onset of seizure and diagnosis/commencement of medications: Late diagnosis and commencement of medications have been found to increase the risk of cognitive decline. Clinical studies showed that cognitive impairments induced by seizures are reversible for most seizure types when seizures are diagnosed early and controlled adequately [15].
- Type of seizure: The risk of cognitive impairment is increased in some seizure types such as focal to bilateral tonic-clonic [16].
- Frequency and Duration of seizure: Cognitive decline has been recognized as a sequel of intractable epilepsy. A number of factors have been identified as having a role, including underlying pathology, seizures and medications. Status epilepticus and frequent recurrent chemically and electrically induced seizures can result in cognitive impairment. In individuals with high seizure frequency, cognitive impairment may have a greater impact on daily life [17].
- Type, dosage, duration and compliance of antiepileptic drugs: Antiepileptic drugs (AEDs), which not only reduce neuronal irritability but may also impair neuronal excitability. The major cognitive effects of AEDs are impaired attention, vigilance, and psychomotor speed, but secondary effects on other cognitive functions can be seen. AED-induced cognitive side effects are increased with rapid initiation, higher dosages and polytherapy [18]. Epilepsy commonly produce changes in cognitive abilities and may even manifest with neuropsychiatric symptoms [19]. The knowledge of the presence and characteristics of these cognitive disturbances can aid in the diagnosis, management and long term care of affected person. Neuropsychological evaluation is one of the methods of garnering quantitative information about cognitive and behavioural changes in patients with known neurological diseases like epilepsy or who are considered to be at risk of brain dysfunction [20].

AIM AND OBJECTIVE

To determine the prevalence of cognitive dysfunction in adult patients with epilepsy using FEPSY and MOCA

RESEARCH QUESTION

What is the prevalence of cognitive impairment in adult patients with epilepsy?

HYPOTHESIS

Prevalence of Cognitive dysfunction is significantly higher among adult patients with epilepsy than those without epilepsy.

METHODOLOGY AND DATA ANALYSIS

STUDY SITES

The study was carried out in the consultants' outpatient clinics and medical wards of the department of Internal Medicine, University of Benin Teaching Hospital (UBTH) Benin and Federal Medical Centre (FMC) Owerri. The institutions are tertiary hospitals located in the Southern part of Nigeria. UBTH is a 550 bedded hospital located in Benin, the capital of Edo State with `geographic coordinates (6.3350^{0}N, 5.6037^{0}E). UBTH serves as major referral centre in Edo State with a population of about 3.2 million people mainly of Bini, Esan, Owan, Afemai and Akoko Edo who speak Edo and derivatives of Edo languages. FMC is a 430 bedded hospital located in Owerri, the capital of Imo State with geographic coordinates (5.4891^{0}N, 7.0176^{0}E). FMC serves as a major referral centre in Imo state with a population of 3.9 million mainly Igbos who speak Igbo language. Although there are other peripheral hospitals that manage epilepsy, most patients in these states are usually referred to UBTH and FMC for further care due to the available expertise. So, the neurology units in these centres could be said to serve these states.

SAMPLE SIZE ESTIMATION

The sample size was determined using the formula of Kish.Using Leslie Kish's formula for a single arm cross-sectional study.Where the prevalence of approximately 100/1000[5]

$N = Z^2$. $P(1-P) /d^2$. Where P = prevalence Z =1.96, d = 0.05, $N = (1.96)^2$ x 0.10(1 – 0.10) / 0.05^2= 3. 8416 x 0.10 x 0.990/ 0.0025 = 0.3803184/ 0.0025= 152

Since the target population is less than 10,000, the sample size was adjusted for finite population correction using the formula, nf = n/(1 + (n-1/N). Where, nf = the desired sample size for population < 10,000, n = the earlier estimated sample size, N = the population size (1000) nf = 152 / 1 + (152-1/1000), nf = 152/1+(151/1000) = 152/1+0.151

= 152/1.151 = 132

To accommodate those patients who did not have complete data (To allow for attrition factor of 15%),Total sample was adjusted to 132 + 18,(15% of 132 = 18). Therefore, the sample size of 150.

FOR THE CONTROL

It was 2 to 1 matching, that is, for every two PWEs there was one control subject matched for age, sex and level of education. The number of controls was 75.

STUDY POPULATION

The study population consisted of cases which were patients with epilepsy attending clinics in consultants' outpatient department (COPD) and those admitted in the medical wards of the department of Internal Medicine UBTH, Benin and Federal Medical Centre Owerri while the controls consisted of mostly healthy subjects that accompanied relatives to the hospital and some hospital staff.

INCLUSION CRITERIA FOR CASES

1. Adult patients with clinically diagnosed epilepsy with or without EEG.
2. Adult patients with epilepsy who gave written informed consent.
3. Adult patients (18 years and above) with epilepsy resulting from unprovoked seizures.

EXCLUSION CRITERIA FOR CASES

1. Patients with epilepsy less than 18 years resulting from unprovoked seizures.
2. Patients with acute symptomatic seizures or from provoked seizures.
3. Patients with medical co-morbidity that will limit the assessment of cognitive dysfunction, for example, dementia.
4. Non consenting patients

INCLUSION CRITERIA FOR CONTROLS

1. Adults (18 years and above) without epilepsy or seizures who gave written informed consent.

EXCLUSION CRITERIA FOR CONTROLS

1. Adults (18 years and above) with epilepsy.
2. Adults with any form of seizures.
3. Adults with medical co-morbidity that will limit the assessment of cognitive dysfunction, for example, dementia.
4. Non consenting adults.
5. Adults with family history of epilepsy.

SAMPLING

All participants with epilepsy, who gave informed consent, and who met the inclusion with none of the exclusion criteria were enrolled consecutively into the study over a period of twelve (12) months.

PILOT STUDY

A pilot study was conducted prior to the main study, to adapt the Montreal Cognitive Assessment (MOCA) tool to the local context and pretest the questionnaire. The pilot study was done to determine cutoffs that will be used for the study participants with regards to the adapted MOCA, in addition to gather feedback which were used to improve the structure and administration of the questionnaire. Thirty (30) participants were assessed using both the original Montreal cognitive assessment (MOCA) and the adapted MOCA tools and cut off score for MOCA obtained. The original MOCA was translated to vernacular (Bini) and back translated to culturally appropriate English. Each of the participants was tested with the original MOCA and then with an adapted MOCA (MoCA[1]) after 3 hours or more. Those with ≤ 12 years of education were added extra one point. The analysis was done by subtracting the 2 x standard deviation from the means (Mean - 2SD) of the original MOCA and that of the adapted version in the 3 batches; the whole group, those with ≥12 years of education and those with ≤12 years of education. The adapted MOCA was then used in the study. Feedback from the pilot study were then used for correction, modification and standardization of the questionnaire.

DATA COLLECTION

150 Patients with Epilepsy (PWE) and 75 controls who met the inclusion criteria were enrolled into the main study. Patients with epilepsy and the controls were coded and their medical case notes were used for further evaluation. Data from each participant was gotten from a standardized proforma, biodata and history of the present illness along with clinical and neurological examination. The diagnosis of Epilepsy was clinical and corroborated with Electroencephalogram (EEG) if available. Seizure frequency is basically classified into three groups namely; those that have more than 1 seizure per month (which depicts that there is more frequent seizures), those that have 1 seizure or less per month (this depicts frequent seizures) and those that have 1-2 seizures per year (this depicts less frequent seizures). Duration of seizures before treatment is divided into two groups namely; those that had seizures for a year or less and those that had seizures for more than one year. Certified and tested cognitive assessment tools; Iron Psychology (FEPSY) for windows version 2.3.3 and adapted MOCA modules were used. The Cognitive assessments were done after the participant had finished filling the

questionnaire. The questionnaire for the data collection and adapted MOCA form are as shown in the appendix. Tests done using FEPSY were Auditory and Visual reactions, Binary choice tasks, Recognition simultaneously and Tapping to assess mental speed, psychomotor speed, attention, memory, constructional praxis respectively. Operationally for this study, cognitive dysfunction was defined as an adapted MOCA of ≤22. Data were dichotomized between normal and cognitive dysfunction using the cut-off of ≤22. FEPSY (scores and mean) were also compared between cases and controls.

ETHICAL CONSIDERATIONS

Ethical approval was obtained from the Ethics committee of UBTH Benin and FMC Owerri. The study was done at no cost to the participants. Informed consent was obtained from all participants in the study.

STATISTICAL ANALYSIS

The data obtained were analyzed using SPSS version 25. Results were presented in tables with data first described using frequency tables. Categorical variables between cases and Controls were compared using chi square and Fisher exact test. Continuous data were compared using ANOVA or its non-parametric equivalent where appropriate. Logistic regression was used to determine the risk factors of cognitive dysfunction in study participants. Operationally for this study, cognitive dysfunction was defined as an adapted MOCA of 22 or below. A p-value < 0.05 was considered statistically significant for all tests.

RESULTS

MOCA ADAPATION

Demographic characteristics

A total of 30 normal subjects participated in this pilot study which comprised of 16 (53.3%) males and 14 (46.7%) females. Among the participants 17 (56.7%) had tertiary level of education, secondary 8 (26.7%), primary 4 (13.3%) and none 1 (3.3%). Age range was between 18 and 40 years with a mean age of 27±SD 6.3 years.

Adaptation of MOCA assessment tool

For those with more than 12 years of education, mean values of original MOCA total and translated MOCA total were 26.06 and 27.55 respectively while their corresponding standard deviation values were 3.73 and 3.02. Using the formula (mean - 2SD), giving 18.60 approximately 19 for original MOCA and 21.53 which is approximately 22 for adapted MOCA.

MAIN STUDY

Demographic characteristics

The demographic characteristics of the study participants are shown in Table 1. The ages of the cases and controls were categorised into <25-, 26-34- and 35-44 years. Participants <25years had the highest proportion both in the cases and the controls [83(55.3%) and 36(48.0%) respectively]. There was no statistically significant difference between the age distribution (p=0.244). The study participants comprised of 82 (54.7%) males and 68 (45.3%) females for the cases and 36 (48.0%) males and 39 (52.0%) females for controls. For the cases and the controls, there was no significant gender difference (p=0.345). The highest level of education of the participants was secondary for both cases and controls, and no significant difference was observed among the categories [120(80.0%) and 56 (74.7%) respectively, p=0.245]. The age distribution of the study participants, gender distribution and the level of education are represented in Figure 1, Figure 2 and Figure 3 below.

Table 1: Demographic characteristics of the study participants

Variables	Cases [n(%)]	Controls [n(%)]	p-value
Age distribution <25 years 26-34 years 35-44 years	 83 (55.3) 62 (41.3) 5 (3.3)	 36 (48.0) 33 (44.0) 6 (8.0)	0.244
Gender Male Female	 82 (54.7) 68 (45.3)	 36 (48.0) 39 (52.0)	0.345
Level of Education None Primary Secondary Tertiary	 3 (2.0) 6 (4.0) 120 (80.0) 21 (14.0)	 0 2 (2.7) 56 (74.7) 17 (22.7)	0.245

Figure 1: A bar chart showing the sex distribution of the cases and controls in the study

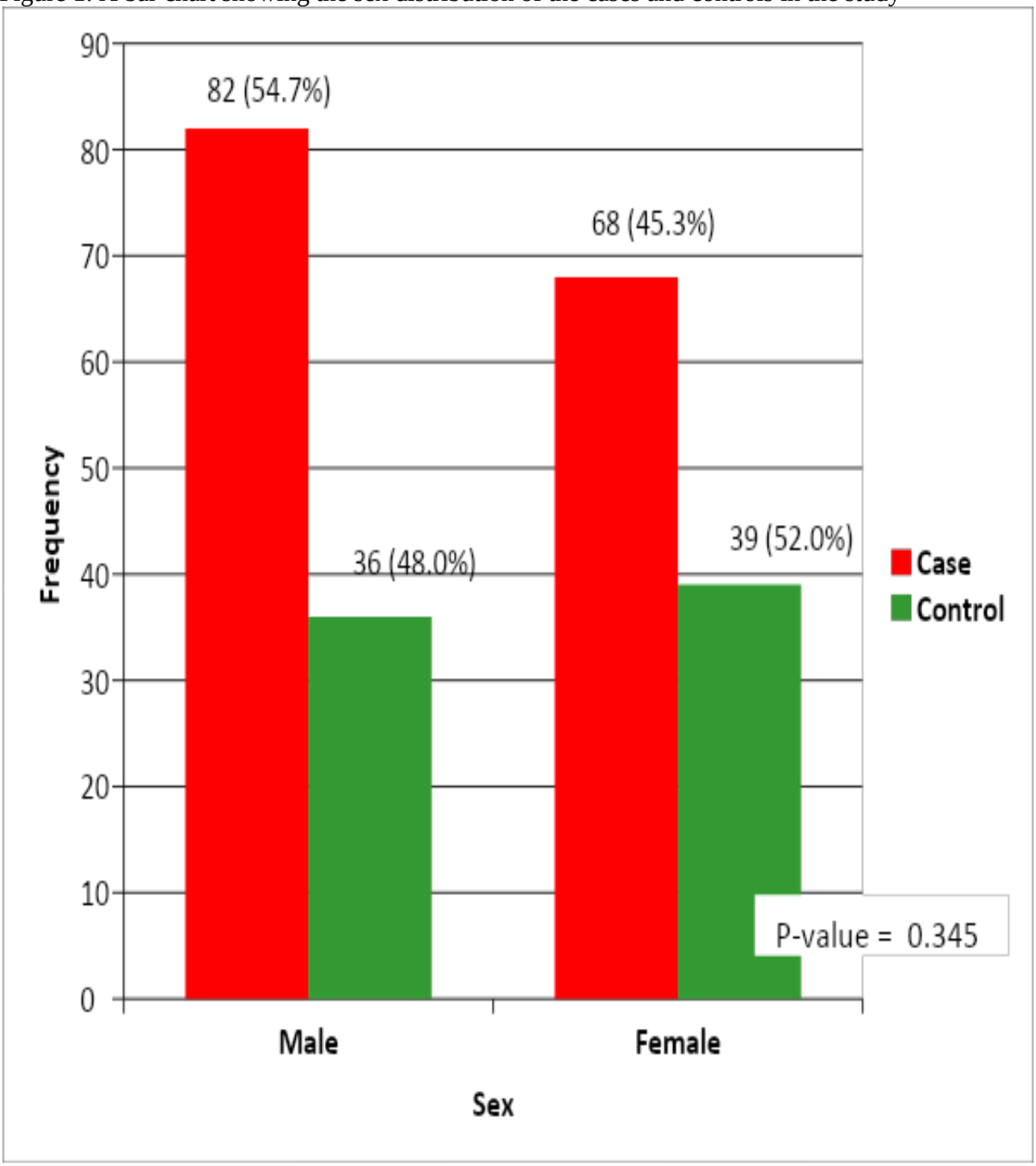


Figure 2: A bar chart showing the age distribution of the cases and controls in the study

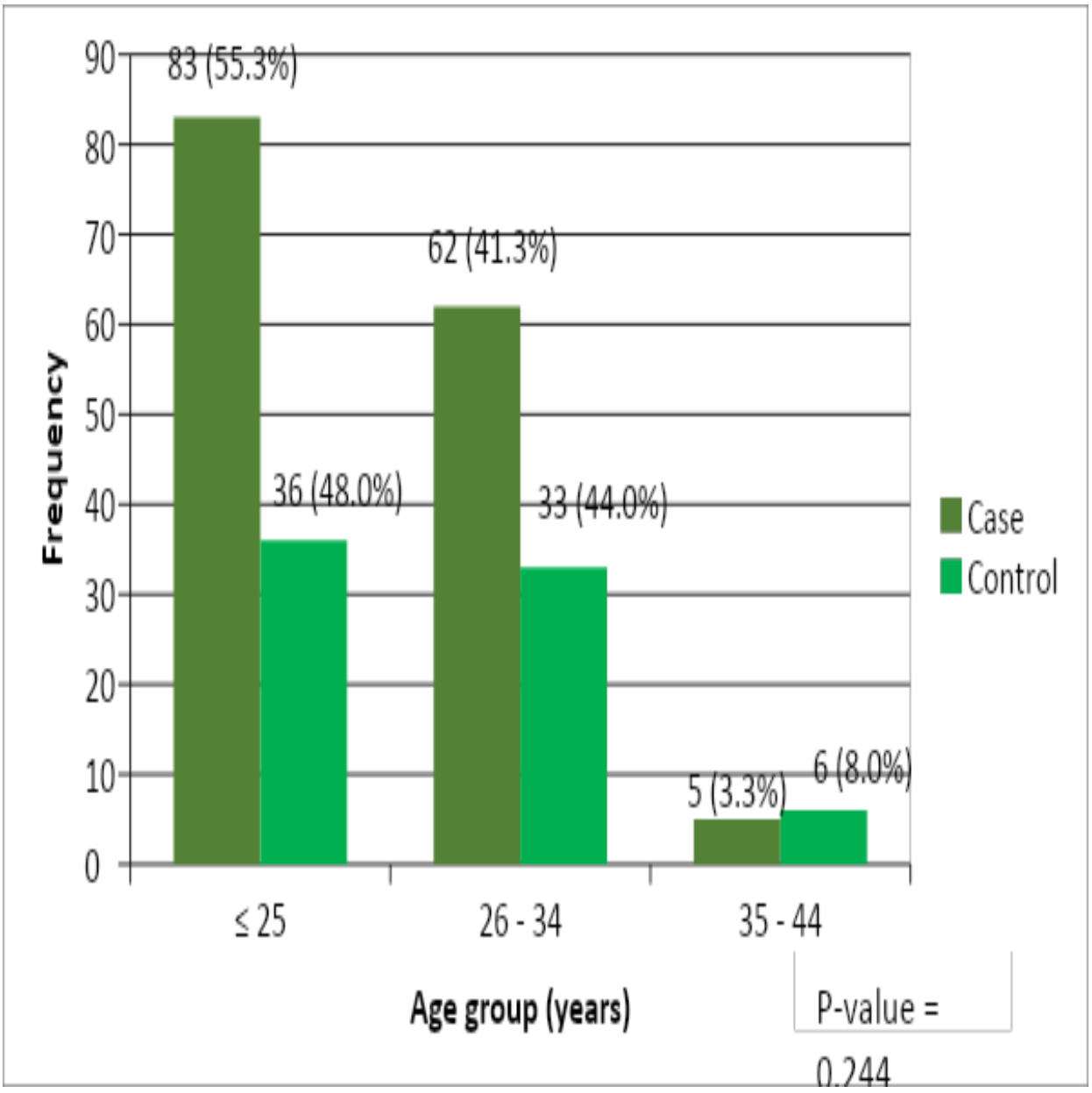
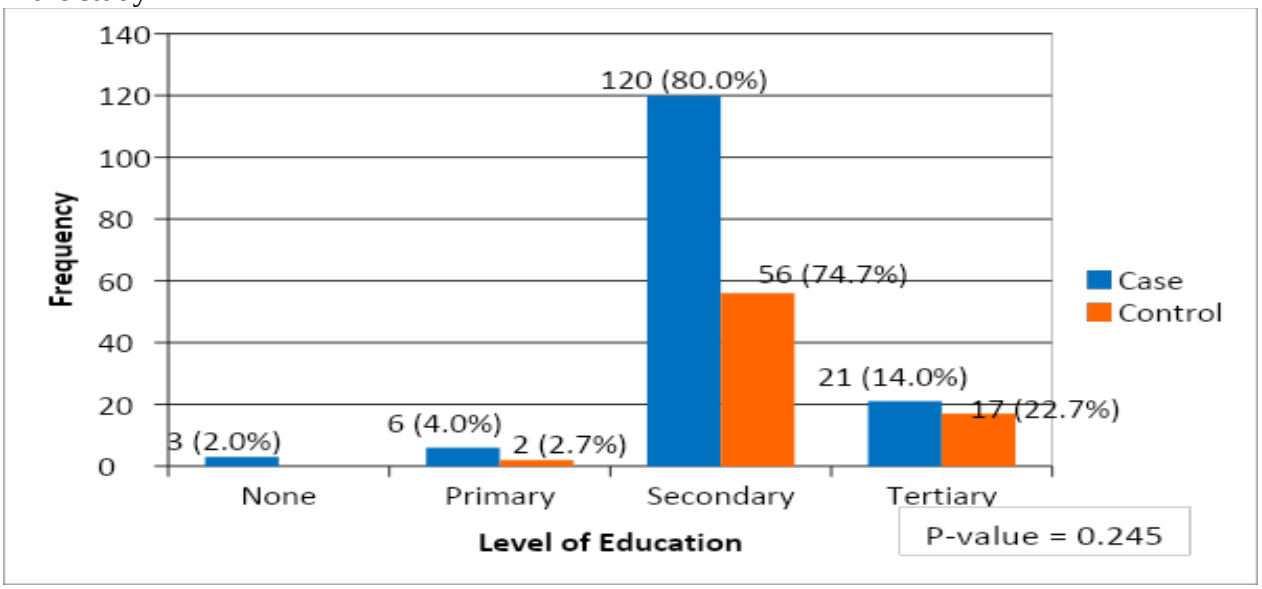


Figure 3: A bar chart showing the distribution of level of education of the cases and controls in the study



PREVALENCE OF COGNITIVE DYSFUNCTION

Frequency table for cognitive dysfunction in the study participants showing the Fisher exact test is illustrated in table 2 below. Using MOCA ≤22 as the cut off, for cases 31 out of the 150 were observed to be cognitively impaired with a prevalence of 20.7%. Among the controls, none was cognitively impaired. This was statistically significant (p<0.005).

Table 2: Frequency table for cognitive dysfunction in the study participants

Variables	Cases (n=150) [n (%)]	Controls (n=75) [n (%)]	p-value
MoCA[1] Score			
<= 22	31 (20.7)	0	<0.005
>22	119 (79.3)	75 (100.0)	

DISCUSSSION

Demographics

The mean age of this study is in agreement with the study done by [21] using community screening interview for dementia (CSID). The important finding from their study was that younger adults suffer more from epilepsy in developing countries [22]. Also, other studies in developing countries, showed a general trend towards a higher prevalence of the disease during adolescence or early adulthood [23]. On the contrary, some studies in developing countries, demonstrated that the prevalence of epilepsy remained stable in the third and fourth decades and typically drops after the fifth decade of life, probably because the studies were carried out in particular age groups [24]. However in the developed countries, most studies show the prevalence of epilepsy to be stable in the adult age groups and increase with age after 50 years [25]. The variance in the age of manifestation of epilepsy between developing and developed countries could be explained by the aetiology. In developing countries, causes of epilepsy include neuro-infections, birth and head injuries and rarely brain tumours commonly found in younger age groups while in the developed countries epilepsy is usually caused by stroke and brain tumours more in adults [26]. In another study, prevalence then again increases after age 60 [27].

This study observed that more males had epilepsy compared to the females, though this was not statistically significant. This finding is consistent with previous studies done with FEPSY in the south-east and south-south of the country [27]. A study done in a developed country also showed that the

prevalence is higher in males than females too. It is thought that, in most parts of Africa and Asia, males more readily go to the hospital for socioeconomic reasons and hence predominate in the hospital populations [28]. Other reasons why there are recorded lower prevalence of epilepsy in females may be explained by poor presentation of females with epilepsy to the hospital as a result of low level of education, african gender roles, fear of stigmatization or deterring marriage [29]. The male sex preponderance may also be due to occupational and social exposure to epileptogenic insults such as cranial trauma and alcohol. Another study conducted in India reported a higher prevalence of epilepsy in males and this was statistically significant. In their population, women with epilepsy are perceived not to be marriageable and this may have led to active concealment of symptoms or diagnosis among these women [30].

The current study observed that the highest level of education among participants was secondary, however level of education was not significant. This may be due to the fact that the prevalence of epilepsy is highest in adolescence [24]. The study was in consonance with the study carried out by [23] using FEPSY but varied from the work done with CSID which may be due to varied location or the neurocognitive assessment tool used [24].

Prevalence

A prevalence of 20.7% for cognitive dysfunction using MOCA was observed in the current study. MOCA as a tool for assessing cognitive dysfunction in PWE has not been widely used. However, prevalence of cognitive impairment using other cognitive assessment tools in evaluating different cognitive domains have been reported [20]. Other studies assessing different domains of cognition noted a high prevalence of cognitive dysfunction among PWE ranging between 14-92% [21, 23, 25]. From the study, there was a statistically significant difference in the performances of the patients with epilepsy when compared with the controls with both cognitive tests. This was in agreement with the studies carried out by [26, 28] in the country. The reason is that the epilepsy as an illness affects the cognition of the patients. Numerous factors such as duration of illness, type and dose of medications, type of epilepsy, frequency of seizures are among other things cause cognitive impairment in patients with epilepsy.

CONCLUSION

In conclusion a high prevalence (20.7%) of cognitive dysfunction among PWE.Early diagnosis of epilepsy, prompt commencement of appropriate and adequate dosage of medications, effective general health promotion are necessary to reduce the prevalence and associated risk factors of cognitive dysfunction.

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