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PREVALENCE AND FACTORS ASSOCIATED WITH DEPRESSION AMONG PATIENTS WITH EPILEPSY AT AGA KHAN UNIVERSITY TEACHING HOSPITAL NAIROBI

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ABSTRACT

Objective: To determine the prevalence and factors associated with depression in patients with epilepsy at Aga Khan University Hospital; Nairobi.

Design: A Cross-Sectional Survey.

Setting: Neurology clinic, Aga Khan University Hospital; Nairobi

Subjects: Eligible patients with epilepsy on follow-up at the neurology clinic were recruited.

Intervention: Beck-Depression-Inventory was administered to evaluate presence of depression.

Main Outcome Measures: In addition to depression, patients with co-morbid depression were further evaluated for associated factors.

Results: Three-hundred-and-twenty-seven patients were evaluated for presence of depression. Fifty-four patients in the study cohort had depression, giving prevalence of depression; based on the Beck-Depression-Inventory as 16.5 %, (95 % CI 12.7-21.0) There was weak association between mild depression and polytherapy (use of two or more antiepileptic drugs), with OR 2.3, 95%CI 0.9-5.8 however, none between polytherapy and moderate or severe depression. No statistically significant association was found between depression and duration of epilepsy or number of seizures per month over last three months.

Conclusion: The prevalence of depression in patients with epilepsy at Aga Khan University Hospital, Nairobi was 16.5 % (95% CI 12.7-21.0) and polytherapy was weakly associated with mild depression. Depression among patients with epilepsy warrants clinical attention especially in patients on polytherapy. The risk of AED polytherapy was two-fold greater (OR 2.3, 95% CI 0.9-5.8) in patients with mild depression compared to patients with epilepsy without depression.

INTRODUCTION

Epilepsy is a condition where one has recurrent and unprovoked seizures occurring 24 hours apart, this being the operational definition adopted by the International League Against Epilepsy (ILAE) for purposes of conducting epidemiological studies in epilepsy (1). International League Against Epilepsy (ILAE) and the International Bureau for Epilepsy (IBE); in 2005, defined epilepsy as brain disorder characterised by an enduring predisposition to generate epileptic seizures and by neurobiological,

cognitive, psychological and social consequences of this condition (1)

Epilepsy is one of the most common chronic neurological disorders, affecting approximately 50 million people worldwide, 40 million of whom are estimated to live in developing countries (2). Estimates from community survey of epilepsy in Kilifi County-Kenya show overall prevalence of active convulsive epilepsy to be 4.5 per 1000 (3)

Throughout recorded medical history, clinicians have observed the strong association between depression and epilepsy. This bi-directional

relationship between depression and neurological disorders was recognised 26 centuries ago by Hippocrates (4). Hippocrates noted in about 400 BC that:

“Melancholics ordinarily become epileptics and epileptics Melancholics: what determines the preference is the direction the malady takes; if it bears upon the body, epilepsy, and if upon the intelligence, melancholy” (5).

It has been found that in patients with refractory epilepsy presence of depression is one of the most important variables that affect their quality of life, even more than the seizure frequency and severity. Boylan *et al* found that depression evaluated using Beck's Depression Inventory was a better predictor of the quality of life than was seizure frequency (6). Complete cessation of seizures remains the paramount goal of therapy in epilepsy; however there is need to better appreciate the importance of co-morbid mood disorders in the overall treatment plan (7).

MATERIALS AND METHODS

This was a cross-sectional survey. Data were collected between September 2012 and February 2013 and data analysis carried out between March and April 2013.

All patients with epilepsy in the study were on follow up at Aga Khan University Hospital Nairobi. Aga Khan University Hospital is a referral tertiary health facility, located in Nairobi, the capital city of Kenya. The hospital runs specialist clinics including the neurology clinic where this study was conducted and receives referrals of patients from throughout Kenya, Eastern and Central Africa.

The neurology clinics are conducted by a consultant neurologist and are held on four days in a week with a work load of twenty to thirty patients in each clinic day. Patients with epilepsy were identified in the clinic according to International League Against Epilepsy (ILAE) definition. These were patients with recurrent, unprovoked seizures and neurobiological, cognitive, psychological and social consequences of this condition.

The study was initiated after appropriate approval had been obtained from the Department of Internal Medicine, AKUHN and the Ethical and Scientific Review Committee.

The objectives of the study were to determine the prevalence of depression among patients with

epilepsy on follow up at Aga Khan University Hospital, Nairobi and association of number of seizures over past three months, polytherapy with antiepileptic drugs and duration epilepsy with occurrence of depression.

The study was designed to determine prevalence of depression with 95% confidence interval. Cochrane, 1963.

Sample size computed for numbers of seizures, polytherapy and duration of seizures were 184, 310 and 220 respectively at 80-90% power based on past studies (8,9,10). Hence the sample size used in the study was 327 patients.

The inclusion criteria consisted of all patients aged ≥ 18 years with epilepsy and on follow up at Aga Khan University Hospital.

The exclusion criteria consisted of those patients who were unable to respond to the study questionnaire due to mental handicap.

After informed consent was obtained, the Beck Depression Inventory-II was administered to patients with epilepsy on follow up at Aga Khan University Hospital. A pretested study questionnaire assessing demographic characteristics of study participant, epilepsy duration, seizure type, frequency and treatment was also administered.

Patients diagnosed with depression were scheduled for psychiatry clinic consultation with a consultant psychiatrist and appropriate care continued.

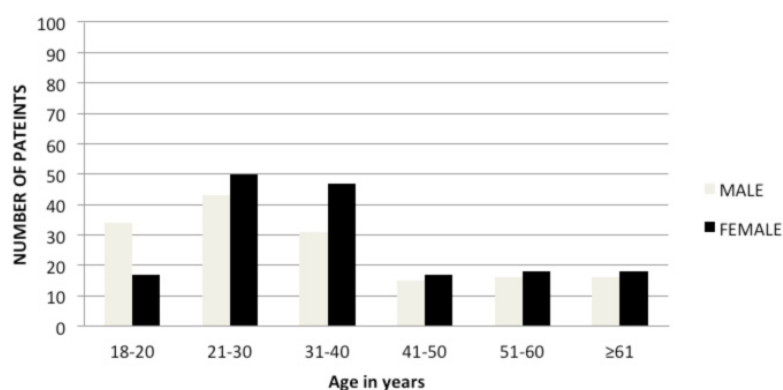
All consenting patients who were on follow up for epilepsy at AKUH neurology clinic during the study period were recruited into the study; hence possibility of selection and sampling bias was reduced. All questionnaires were completed by the primary investigator.

Data were analysed using the Statistical Package for Social Sciences (SPSS) version 17 for descriptive and inferential statistics.

RESULTS

A total of 327 patients with epilepsy on follow up at AKUHN were recruited into the study. The average age of study participants was 35.6 years (15.4) and 176 (54%) patients were females, as shown in Figure 1. Most (96.3%) of the patients were African. One hundred and ninety-three (58.8%) patients were married and 184 (56.1%) were employed.

Figure 1
Age and Gender distribution of patients with epilepsy at AKUHN



Most patients with epilepsy presented with generalised convulsive seizures, 269 (82.5% [95% CI 77.7-86.2]), and 39 (12%) (95% CI 8.6-15.9) presented with complex partial seizures. Nineteen patients (5.8%) presented with simple partial seizures.

Most n= (98.8%) patients were on antiepileptic medication. The duration of treatment ranged from

less than a year to 10 years and 40.7% of patients had been on treatment for durations between a year and three years. Seventy five percent of patient on treatment were managed using a single antiepileptic drug and the drugs were most commonly (56.8%) administered once a day. Table 1 presents details of epilepsy treatment for patients in the study.

Table 1
Pharmacological management of patients with epilepsy at AKUHN

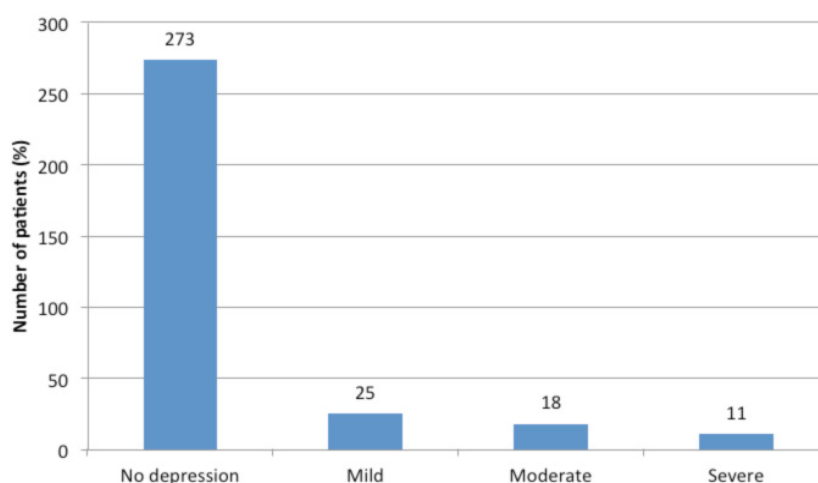
| Characteristics | Frequency (%) |
|--|---------------|
| Ever taken medications to control seizures | 324 (98.8%) |
| Duration on seizure medication (in years) | |
| < 1 | 113 (34.9%) |
| 1-3 | 131 (40.7%) |
| 4-5 | 38 (11.5%) |
| >5 | 42 (12.9%) |
| Types of treatment | |
| Single drug | 245 (75.5%) |
| Two or more drugs | 79 (24.5%) |
| Daily frequency of drug administration | |
| Once | 184 (56.8%) |
| Twice or more | 140 (43.2%) |

The most frequently prescribed drug for control of seizures was valproate with 40.2% of patients being put on this medication. Sixty-seven (20.4%) patients were treated using carbamazepine and 74 (22.6%) used lamotrigine.

The prevalence of depression based on the BDI

was 16.5% (95% CI 12.7-21.0) representing a total of 54 patients with depression in the 327 patients with epilepsy at AKUHN. Figure 2 shows the severity of depression in the 54 patients with depression as a subset of the total study population.

Figure 2
Depression diagnosis according to severity among patients with epilepsy at AKUHN



Univariate analysis was done using the SPSS version 17 and bivariate analysis with the chi square test was used to analyse for relationship between depression and treatment (polytherapy or monotherapy), duration of epilepsy and number of seizures experienced. Depression diagnosis was not significantly associated with either patient age ($p = 0.11$) or gender ($p = 0.35$). Patient gender was not statistically associated with depression diagnosis. Twenty eight (18.7%) males had depression compared to 26 (14.7%) female patients ($p = 0.35$).

Table 2 shows the association between antiepileptic drug therapy and depression in patients with epilepsy. There was a weak association between AED polytherapy and mild depression ($p = 0.048$) but AED therapy did not show a significant association with either moderate ($p = 0.29$) or severe ($p = 0.71$) depression. The risk of AED polytherapy was two-fold greater (OR 2.3, 95%CI 0.9-5.8) ($p = 0.048$) in patients with mild depression compared to epileptic patients without depression.

Table 2
Depression and AED polytherapy in epileptic patients at AKUHN

| | AED | | OR (95% CI) | P-value |
|---------------------|-------------|-------------|----------------|---------|
| | Monotherapy | Polytherapy | | |
| No depression | 210(85.6%) | 60 (76%) | 1.0 | |
| Mild depression | 15 (6.2%) | 10 (12.7%) | 2.3 (0.9-5.8) | 0.048 |
| Moderate depression | 12 (4.9%) | 6 (7.6%) | 1.7 (0.5- 5.2) | 0.29 |
| Severe depression | 8 (3.3%) | 3 (3.8%) | 1.3 (0.2-5.6) | 0.71 |

As shown in table 3, the severity of depression diagnosis did not show a significant association with the duration of epilepsy. Eighty-two percent of patients with short durations of illness (< two years) and 84.6% of patients with epilepsy with duration of illness longer than two years did not have depression.

Table 3
Depression and duration of epilepsy in patients at AKUHN

| | Duration of epilepsy | | OR (95% CI) | P-value |
|---------------------|----------------------|--------------|----------------|---------|
| | < 2 years | ≥ 2 years | | |
| No depression | 126(82.4%) | 147 (84.4 %) | 1.00 | |
| Mild depression | 9 (5.9%) | 16 (9.1%) | 1.5 (0.6-4.0) | 0.34 |
| Moderate depression | 10 (6.5%) | 8 (4.6%) | 0.7 (0.2- 2.0) | 0.43 |
| Severe depression | 8 (5.2%) | 3 (1.7%) | 0.3 (0.1-1.4) | 0.08 |

The frequency of seizures among patients with epilepsy was not significantly associated with depression Table 4. The risk of one or more seizure in the three month period prior to the study were 1.9 times higher (95 %CI 0.8-4.9) in patients with mild

depression compared to those with no depression. The odds ratio for seizures in moderate and severe depression were 1.0 (95% CI, 0.3-2.8) and 1.8 (95% CI, 0.4-7.8), respectively.

Table 4
Depression and self reported frequency of seizures in patients at AKUHN

| | Number of seizure per month | | OR (95% CI) | P-value |
|---------------------|-----------------------------|-------------|----------------|---------|
| | None | One or more | | |
| No depression | 164 (85.7%) | 109 (80%) | 1.00 | |
| Mild depression | 11(5.8%) | 14 (10.4%) | 1.9 (0.8-4.9) | 0.12 |
| Moderate depression | 11 (5.8%) | 7 (5.2%) | 1.0 (0.3- 2.8) | 0.94 |
| Severe depression | 5 (2.6%) | 6 (4.4%) | 1.8 (0.4-7.8) | 0.33 |

There was no impact of seizure type, including general seizures and complex partial seizure on depression. (p=0.84)

DISCUSSION

The patients demographic characteristics evaluated, in comparison to those of other studies conducted on patients with epilepsy included patients age and gender. Like many similar studies conducted on patients with epilepsy, this study was conducted on a strictly adults only population. With respect to the age of patient in this study, the average age of patients in this study was 35.6 years, this age being older than of patients in a previous study by Fotaye *et al*, who found study participants had a mean age of 27.6 years (11). Whereas regarding gender, 46% of patients in this present study were male. Ogunrin in Benin City had similar gender distribution as this present study with 47% of the study participants of male gender. This study reported higher Beck Depression Inventory scores among female study participants (12). However, this present study did not report an association between depression and female gender.

With respect to the socio-economic status of the study participants, of the patients in the study, 18% were unemployed. Unemployment itself has been found in some studies to be a strong contributor to depression among patients with epilepsy; such as in a study conducted in U.K, where a much higher number (49%) of patients were not in paid employment. In this study, the factors found pertaining to lack of employment included epilepsy itself as well as employer attitude to epilepsy. The UK study had a prevalence of depression of 11.2%, less than the present study (13).

Regarding the seizure types encountered in this study, 12% presented with complex partial seizures. The percentage of patients in this present

study with complex partial seizures was lower than that described by Grabowska-Grzyb *et al* in a study conducted in Poland, which had 58% of subjects having complex partial seizures, and depression was associated with complex partial seizures in the Poland study. Grabowska-Grzyb *et al* found a much higher prevalence of depression (49%) than this present study, which finding may be explained by the much higher number of complex -partial seizures in the study participants (14).

Concerning the epilepsy treatment of the subjects in this study, 75% patients on treatment were managed using a single antiepileptic drug. This group on monotherapy was similar to that in a study conducted at Ile-Ife Nigeria where 69.9% patients with epilepsy were on single agent (8). The most frequently prescribed drug for control of seizures was valproate in 40.2% of patients. This is in keeping with the National Institute for Health and Clinical Excellence 2012 Guidelines on diagnosis and management of epilepsy in adults where valproate is the recommended first line therapy for generalised tonic clonic seizures.

A key finding in this study is that eighty three percent of patients in this present study were on medication found in some studies to have beneficial effect on depression such as valproate, lamotrigine and carbamazepine (16,17). The use of these medications may have contributed to the lower prevalence of depression in this present study compared to other studies; however, on sub analysis of the data with regard to specific antiepileptic treatment no significant association was seen with valproate, carbamazepine and depression diagnosis.

One of results in the present study was on the association between AED polytherapy and mild depression, though weak (p = 0.048). Furthermore, the risk of AED polytherapy was two-fold greater (OR 2.3, 95% CI 0.9-5.8) in patients with mild depression

compared to epileptic patients without depression. Similar findings to the present study were observed by Dias *et al*, with association between depression score and number of antiepileptic drugs with lowest scores found in patients on monotherapy. It was thought that the association between the number of antiepileptic drugs and occurrence of depression was more an association between depression and seizure activity, with several antiepileptic drugs likely indicative of more difficult to control seizures (17).

With respect to the duration of epilepsy found in the study participants, similar prevalence of depression was found in the patients with shorter, and longer duration of epilepsy in this present study, where a cut-off of two years was used. These results are in contrast to the findings of Fotaye *et al* who found association between duration of epilepsy and occurrence of depression, with those having durations of epilepsy of more than ten years having more reports of depression. The difference between these results and the conclusion of this present study may be explained by the longer duration of ten years as compared to two years in this present study (11).

In conclusion, the study found that prevalence of depression based on BDI was 16.5%, representing a total of 54 patients diagnosed to have depression in the study population of 327 patients with epilepsy at AKUHN.

This prevalence is lower than other local and regional studies. This low prevalence of depression may be attributed to low prevalence of complex partial seizures (12%) known to be associated with depression. In addition, 83.2% patients in this present study were on medication found in some studies to have beneficial effect on depression such as valproate, lamotrigine and carbamazepine.

However, depression among patients with epilepsy warrants clinical attention especially in patients on polytherapy. The risk of AED polytherapy was two-fold greater (OR 2.3, 95% CI 0.9-5.8) in patients with mild depression compared to patients with epilepsy without depression.

The implications of the results of this study in management of the patient with epilepsy are that physicians attending to patients with epilepsy should routinely screen for depressive symptoms especially among those on more than one anti-epileptic drug.

The limitations of this present study are mainly that owing to the sample size, the impact of some epilepsy related and social factors on depression in epilepsy could not be adequately assessed, and the study focused on the three factors that the sample size provided adequate numbers for evaluation.

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