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Research Article

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Management of epilepsy at a public tertiary hospital in Ghana

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Abstract Epilepsy is a condition characterized by repeated seizures due to a dysfunction of the brain cells. This study helped to determine appropriateness of drug treatment, availability and easy access to medication at the Komfo Anokye Teaching Hospital (KATH), Kumasi. In addition, patients were assessed for the presence of depression as comorbidity.

The study reviewed 164 patient folders and interviewed 70 patients using a questionnaire. Patients who visited the hospital from January, 2013 were included in the study. Data collected included demographic data, epilepsy treatment, adverse drug reactions (ADRs). Patients were also assessed for depression.

Patients were between ages 1 to 65 years. Generalized seizures accounted for 93.9%, of which 126 patients presented with tonic-clonic seizures. Six AEDs were commonly prescribed. Carbamazepine was the most prescribed for generalized seizures. For partial seizures, phenytoin was the most prescribed. Eleven adverse drug reactions (ADRs) were reported; the most common being weight gain and headache. 68% of patients purchased their drugs from community pharmacies, whiles 32% received their drugs from the hospital under the National Health Insurance Scheme. 49 patients were positive for depression using the Neurological Disorders Depression Inventory for Epilepsy (NDDI-E) instrument.

Management of epilepsy in KATH is inadequate.

Keywords Epilepsy, Carbamazepine, KATH, antiepileptic drug (AED), adverse drug reactions, NDDI-E

Introduction

Current research has projected an increase in mental health disorders in Ghana as a result of the recognized stresses of industrialization and acculturation [1]. Mental health is, however, a highly neglected area in the Ghanaian health care system [2]. Consequences of poor mental health include predisposition to a variety of physical illnesses resulting in a reduction of the quality of life and lower individual productivity. This in turn affects total national output [3]. Epilepsy is a common neurological condition that often presents with psychiatric/psychological components. 80% of epileptic patients worldwide are known to reside in developing countries [4]. Regardless of this known fact, epilepsy care in developing countries is limited [5]. Several reasons may account for this situation.

The distribution of healthcare resources in developing countries is characterized by obvious inequalities [6]. Private health care facilities provide first class care in contrast to public health facilities. Even these underfunded public health facilities are unequally distributed within the country biased towards urban areas [5]. Access to technological aspects of care is also either totally non-existent or unequally distributed. The application of electroencephalography and neuroimaging (EEG machines, CT and MRI scanners) to assist in the diagnosis and management of epilepsy is extremely limited in many parts of Africa [7]. These may be owned by public hospitals but not employed in diagnoses and tracking of patient progress because the costs involved have to be borne by the patient. It is possible that the lack of medical infrastructure leads to a greater exposure of individuals to common risk factors of epilepsy. These may include birth injury as a result of poor obstetric care [5]. Inadequate health infrastructure is further compounded by a lack of primary health workers and neurologists trained to diagnose and treat epilepsy. There is further the insufficient supplies and high costs of antiepileptic (AED) medications [8].

In times past, epilepsy was thought to be a condition demonstrative of an evil state of mind or possession by spirits [9]. In some cultures, epileptic patients are still considered as people who are inhabited by contagious spirits [10]. Social stigma, misinformation and traditional beliefs affect health seeking behaviour of patients.

The inadequacies in management of epilepsy lead to underdiagnosing of comorbid psychological conditions such as depression. This might result in the deterioration of the underlying epileptic syndrome.

Depression is a common comorbidity with epilepsy. It has an estimated prevalence of between 20–55% in those with chronic epilepsy. Depression is mostly treatable but is often underdiagnosed or overlooked by neurologists and primary-care physicians in patients with epilepsy. Depression is a major cause of suicide ideation and self-injury and an overall reduction in the quality of life of patients with epilepsy. Hence, it is important for it to be detected and managed [11].

This study, therefore, sought to investigate the management of epilepsy in the KomfoAnokye Teaching Hospital (KATH), Kumasi, Ghana is by focusing on the prevalent epilepsy syndromes and pattern of prescribing. Additionally, it sought to investigate the prevalence of major depression in patients with epilepsy at KATH.

Materials and Methods

Data Collection

This study was carried out between August, 2013 and April, 2014. Both prospective and retrospective studies (starting from January, 2013) were carried out. A survey questionnaire was administered to epileptic patients of the Department of Psychiatry at the Komfo Anokye Teaching Hospital, Kumasi through a face- to-face interview. The questionnaire was presented to the patients during their clinic days. Only patients to whom the research procedure was vividly explained and willingly gave their consent were interviewed. The anonymity of the patients was upheld.

A retrospective analysis of a hundred and sixty-four epileptic patients' folders was carried out after the necessary consent was sought. Only patients diagnosed with epilepsy and treated with an AED were included in this study. The following data were obtained from the patients' medical records: demographic data (age and gender), type and aetiology of epileptic seizure and AED prescribed. Random sampling of patients at the Department of Psychiatry was used. The Neurological Disorders Depression Inventory for Epilepsy (NDDI-E) instrument was administered to patients interviewed to screen for the presence of depression as comorbidity. NDDI-E is a self-administered instrument which consists of 6 items rated by a four-point scale ranging from "never" (score = 1), "rarely" (score = 2), "sometimes" (score = 3), to "always or often" (score = 4). The score was obtained by computing the sum of the scores obtained by the items. The possible overall score ranges between 6 and 24. NDDI-E scores above 15 are considered positive for depression. This has a specificity of 90%, sensitivity of 81%, and positive predictive value of 0.62 for a diagnosis of major depression based on the mini international neuropsychiatric interview (MINI)[12].

Ethical approval with reference number CHPRE/AP/130/14 was obtained from the Committee on Human Research, Publications and Ethics (CHPRE) of the School of Medical Sciences, Kwame Nkrumah University of Science and Technology (KNUST), Kumasi, Ghana.

Data analysis

Descriptive data analysis was done using the Statistical Package for Social Sciences (SPSS) and Graph Pad Prism version 6. Descriptive statistics of the categorical (frequencies and percentage) and continuous variables (mean and standard deviation) were calculated. Categorical variables between the group with depression and the group without depression were compared using the Pearson chi-square test and Fisher's exact test, while continuous variables were compared using the Student t-test and Mann–Whitney Utest. *P* values <0.05 were considered significant. Variables in the univariate model were analysed in a multiple logistic regression model to assess potential independent factors and confounders for depression. Odd ratios were calculated with 95% confidence intervals (CI).

Results

Patient characteristics

Data of 164 patients was reviewed; all were outpatients. The age group with the highest number of patients was between 21 to 30 years and most seizures were found to have started between the ages 3 to 17 years. Generalized seizures accounted for almost 93.9% followed by partial seizures (6.1%). Of the generalized seizures, 126 patients presented with tonic-clonic seizures.

Table 1: Demographic and clinical characteristics of the study population (n=164)

Characteristics	Number of patients	Percentage (%)
Gender of patient		
Male	76	46.34
Female	88	53.66
Age group of patient (years)		
1-6	5	3.05
7-14	27	16.46
15-20	8	4.88
21-30	48	29.27
31-40	28	17.07
41-50	16	9.76
51-65	26	15.85
≥ 65	6	3.66
Age of onset of seizures		
≤ 1	24	14.63
1-3	26	15.85
3-11	50	30.49
12-17	50	30.49
18 and above	14	8.54
Seizure type		
Tonic-clonic	126	76.83
Status Epilepticus	8	4.88
Partial Complex Epilepsy	10	6.10
Absence seizure	11	6.71
Tonic	9	5.49
Other factors		
Family history of epilepsy	49	29.87
Low birth weight	11	15.71
Diagnosis		
By primary care physician	67	95.71
Neurologist	3	4.29

AED utilization pattern

Six (6) different AEDs were commonly prescribed for patients assessed during the study period. For generalized seizures except absence seizures, carbamazepine was the most prescribed AED followed by diazepam and phenobarbital. For partial seizures, phenytoin was the most prescribed AED. The details of AED usage in different types of seizures are presented in Table 2. 73 patients were on combination therapy as against 91 who were on monotherapy. 8 patients were on olanzapine and benztropine in addition to their antiepileptic drugs.

Table 2: AED utilization pattern of epileptic patients visiting the Psychiatry department in KATH

Drug	Tonic-Clonic	Status Epilepticus	Partial Complex Epilepsy	Absence seizures	Tonic	Total
Diazepam	10	8	-	5	-	23
Carbamazepine	105	-	5	-	9	119
Topiramate	-	-	6	-	-	6
Sodium Valproate	5	-	-	6	-	11
Phenytoin	8	-	6	-	-	14
*Olanzepine**	-	-	8	-	-	8
*Benztropine**	-	-	8	-	-	8
Phenobarbital	18	-	-	-	-	18
Combination therapy	65	-	8	-	-	73
Monotherapy	61	8	2	11	9	91

*Patients also presented with Epilepsy psychosis.

Drug Related Problems

Eleven common adverse drug reactions (ADRs) were reported from 70 patients. Some patients developed more than one. The most common ADRs were weight gain and headache. The following ADRs were reported in relation to sodium valproate: weight gain, sleep disturbances, fatigue and dizziness. These ADRs were in relation to carbamazepine: headache, dizziness, loss of appetite, sleep disturbances and weakness. Phenytoin ADRs included high blood sugar while patients on topiramate lost weight and those on benztropine had blurred vision.

Table 3: Adverse drug reactions (ADRs) presented by epileptic patients visiting the Psychiatry Department in KATH

Adverse Effect	Number of Patients	Percentage (%)
Weight gain	53	75.71
Weight loss	11	15.71
Fatigue	28	40
Loss of appetite	11	15.71
Weakness	7	10
Headache	42	60
Blurred vision	19	27.14
Chest pain	12	18.57
High blood pressure	30	42.85
Elevated blood sugar	7	10
Sleep disorders	10	14.29

Economic Factors

67.5% of patients interviewed purchased their drugs from community pharmacies whiles 32.5% received their drugs from the hospital under the National Health Insurance Scheme (Table 5). The 67.5% that purchased their own drugs spent between GH¢ 10 and GH¢ 70 monthly on their medication. Table 4 summarizes amounts spent on medication.

Table 4: Amount of money spent on purchasing AEDS by epileptic patients visiting the psychiatry department in KATH

Amount (Ghana Cedis)	Number of Patients	Percentage (%)
10-20	51	31.10
21-30	17	10.37
31-40	51	31.10
41-50	11	6.71
51-60	25	15.24
61-70	9	5.49

Table 5: Availability of medication at the hospital (KATH) for free or community pharmacy (Pharmacy) for purchase by epileptic patients visiting the Psychiatry department in KATH.

Source of AED	Number of patients	Percentage (%)
KATH Pharmacy	47	67.14
Community Pharmacy	23	32.86

Screening For Major Depression

Mean response on the NDDI-E was highest for the item 'Nothing I do is right'. The most frequent score selected by patients was 3.0 (Table 7). Forty-nine (70%) of patients receiving the NDDI-E were screened as positive for depression. These patients had not been previously diagnosed or treated for depression. The mean NDDI-E score of the patients screened was 13.37 (median = 13). 24.48% (n= 12) of the 49 had family history of psychological conditions. Risk factors associated with depression diagnosed with the NDDI-E in the univariate analysis included a family history of psychological conditions ($p<0.001$) and seizure type (tonic-clonic; $p< 0.0039$). Gender, age and use of multiple AEDs were not significantly associated with depression in the univariate model. Tables 8 show the univariate analyses for patients receiving the NDDI-E. Adjusting for confounding factors in multivariate analysis further confirmed a family history of psychological conditions ($p=0.012$) was independently associated with depression.

Table 6: Frequency of responses for each item of the NDDI-E.

Item	Never(1)	Rarely (2)	Sometimes (3)	Always/ often (4)
Everything is a struggle	13	32	21	4
Nothing I do is right	5	20	35	10
Feel guilty	32	10	26	2
I'd be better off dead	58	8	2	2
Frustrated	8	16	45	1
Difficulty finding pleasure	16	6	36	12

Table 7: Statisticsof responses for each item of the NDDI-E.

	Everything is a struggle	Nothing I do is right	Feel guilty	I'd be better off dead	Frustrated	Difficulty finding pleasure
Mean	2.23	2.76	1.96	1.26	2.54	2.63
Std. Error of Mean	0.10	0.09	0.12	0.08	0.09	0.12
Median	2.00	3.00	2.00	1.00	3.00	3.00
Mode	2.00	3.00	1.00	1.00	3.00	3.00
Std. Deviation	0.82	0.79	0.97	0.65	0.72	1.02

Table 8: Univariate analysis of patients receiving the NDDI-E

	NDDI-E>15 (n=49)	NDDI-E≤15 (n=21)	*P*Value
Gender *n* (% female)	30 (61.22%)	11 (52.38%)	0.5986
Age (mean±SD)	33.08±16.78	32.08±15.52	0.8161
Seizure type*n* (% tonic-clonic)	42 (85.71%)	7 (33.33%)	0.0039**
Combination therapy*n* (%)	36 (73.46%)	13 (61.90%)	0.3977
Family History*n* (%)	12 (24.48%)	20 (95.23%)	< 0.001***

SD= Standard deviation

Table 8: Multivariate analysis

	Odd ratio (OR)	Confidence Interval (CI)	*P* Value
Gender	3.29	0.59-18.40	0.174
Seizure type	0.78	0.19-3.27	0.732
Combination therapy	1.70	0.27-10.57	0.574
Family History	**0.20**	**0.06-0.70**	**0.012**

Discussion

Various epidemiologic studies of epilepsy have indicated that, overall, epilepsy is slightly higher in males than in females [13,14]. Various sex ratios have even been reported for individual seizure types [14]. In this study, female numbers (53.66 %) were found to be slightly more than that of males (46.34%). The higher female numbers observed contradicts previous findings even though some describe a female predominance [15]. It may, however, be due to higher health seeking behaviour of the females. The women appeared more interested in their health issues and more likely to seek medical help for health conditions than males. Given the stigma attached to the condition, the chances of under-reporting, though, may be high; the picture on the ground may not, in fact, be a true reflection.

The incidence of epilepsy is believed to be highest during childhood [16]. A similar pattern was observed with our study population; about 91.5% of the population had childhood onset of epilepsy. Risk factors for development of epileptic syndromes in childhood include, among others, head trauma during or shortly after birth as well as intracranial infections and genetic factors [17]. Inherited forms of epilepsy, as shown by numerous studies account for about 20% of all patients with epilepsy, particularly in children [18]. In this study, 29.87% of the patients had a family history of epilepsy. Even though none of the patients had ever presented with previous head injuries, 15.71% had low birth weights. An association between low birth weight and the risk of epilepsy has been established particularly within the first five years of life. This is believed to be due to the susceptibility of the immature brain to seizures when exposed to risk factors [19,20]. A similar pattern was seen in this study as 45% of patients with low birth weight developed seizures within the ages 1-5.

Classification of seizures and epilepsy syndromes is very important. Proper classification relies on detailed patient history, thorough neurologic examination and specialized tests—notably electroencephalography (EEG) and neuroimaging [21]. Correct classification will allow for optimal pharmacological therapy of the disorder and prognosis. Majority of the study subjects presented with generalized seizures as against partial seizures. Majority (95%) of the study population also had their diagnosis done by a primary care physician. Only 5% had had contact with a neurologist previously. It is therefore highly likely that most of the patients had improperly diagnosed and classified epilepsy. EEG is one of the diagnostic tools that help in differentiating the various types of epilepsy syndromes. EEG examination at KATH is expensive but not covered by the National Health Insurance Scheme (NHIS). Since most patients are unable to afford it, full diagnosis may not be done. This may lead to pharmacotherapy that may rather exacerbate their condition and cause other adverse drug reactions.

Most of the epileptic patients were being managed with conventional AEDs like carbamazepine, phenytoin, phenobarbital and sodium valproate. Carbamazepine was the drug most frequently prescribed; mostly for tonic-clonic seizures. The reason for high use of carbamazepine was its lower cost with free supply at public hospitals under the NHIS. For partial seizures, the most frequently used AED was phenytoin. Olanzepine, which is an atypical antipsychotic, was also prescribed for some patients with partial seizures as these patients also presented with epilepsy psychosis as comorbidity. For patients who presented with extrapyramidal symptoms resulting from olanzapine use, benztropine was administered. Topiramate, on the other hand, was prescribed mainly as add-on therapy. Monotherapy was employed for 91 patients while 73 patients were on combination therapy. This was dependent on how well the seizures were under control.

Antiepileptic drugs are supposed to be tailored for each individual syndrome but due to the inconsistent availability of the drugs at the hospital, drugs were given empirically. Ideally, the choice of antiepileptic drug for each patient should be based on seizure type and/or syndrome as well as the individual person's needs. Unfortunately, in most developing countries both the choice and supply of drugs are limited [22]. In the treatment of absence seizures, carbamazepine is the least preferred due to ability to exacerbate seizures [23]. However, data gathered showed that it was still prescribed by some of the physicians.

Most adverse effects of the AEDs reported by the patients were predictable, dose dependent, and easily explained by the known pharmacological properties of the individual medicinal agents [24]. No change of medication was made in any of the cases, as these ADRs were mild. Some patients refused the recommendation to modify medication because they were getting their drugs for free.

Inconsistent availability of antiepileptic drugs at KATH may be due to the fact that epilepsy is not considered a major condition of public health importance in Ghana. Hence, issues relating to its management are not prioritized as compared to conditions such as malaria. Prioritization may be inevitable mainly due to insufficiency of health resources [25]. In view of such problems concerning the supply of antiepileptic drugs, it has been argued that the non-availability of AEDs in health facilities is the most important hindrance to the care of patients with epilepsy [26,27] .

Since most of the drugs supplied under the NHIS were usually not available in the hospital, patients had to acquire them from community pharmacies. Due to high cost of these antiepileptic drugs and inability of some patients to purchase them, there are compromises made in the prescription of drugs by the clinicians. This may not be of high benefit to the patients. A few patients admitted to defaulting on their medication when they were unable to obtain them.

Newer antiepileptic drugs have been introduced that offer significant advantages in terms of their tolerability, favourable pharmacokinetics and lower potential for drug interactions [28]. Per data collated, new generation antiepileptic drugs were not usually prescribed at the Department of Psychiatry, KATH. This according to the physicians in the department was due to the fact that the newer generation AEDs had not been included in the Standard treatment guidelines of the Ministry of Health (MOH), Ghana. As a result of this, these drugs are not catered for by the NHIS. This implies that patients would have to purchase them at high prices form community pharmacies. The only new generation AED encountered was topiramate which had been prescribed to a handful of patients.

A visit to four major pharmacies in Kumasi attested to the fact that new generation drugs were not frequently patronized. Available drugs at these facilities were phenobarbital, carbamazepine, sodium valproate, phenytoin, diazepam and oxcarbazepine; phenobarbital and sodium valproate were the most patronized medicines.

Financial constraints on the part of the patients was identified as the reason for the pattern of purchase. Most patients complained about the cost of the drugs prescribed for them. Hence, the doctors found it inappropriate to prescribe drugs above the financial capability of the patients even if they were better options.

In this study, 49 (29.87%) of the patients were found to have major depression, based on the NDDE-I score. This is similar to prior reports, where rates of major depression in patients with epilepsy ranged between 17.2% and 55% [11]. Chronic disorders can predispose a patient to clinical depression and hence a concern in epilepsy. Epilepsy has also been shown to be a risk factor depression and vice versa [29,30].

Family history of psychological conditions was related to NDDI-E scores consistent with depression which was the strongest independent predictor for depression [OR 0.20 (CI, 0.06-0.70)]. This goes to show that epileptic patients need to be screened for comorbid neurological conditions such as depression even if the conditions are not readily manifested. All patients determined to have depression were not previously diagnosed or treated for depression. The use of anti-epileptic drugs can contribute to depression. Some AEDs such as topiramate have been shown to have negative effects on mood [31]. The use of combination therapy may lead to the manifestation of many negative neurocognitive effects associated with AEDs, one of which may be depression [32,33]. In our study, however, the use of more than one AED was not significantly associated depression. Tonic-clonic seizures were significantly associated depression. This is in contrast to a previous study that found that epileptic patients with depression had significantly lower numbers of generalized tonic-clonic seizure patients, decreased frequency of generalized tonic-clonic seizures. However, had more patients with depression that were on multiple anticonvulsant medications[33].A limitation of this study is that this population is not fully representative of the broader population of patients with epilepsy. Patients with epilepsymight have higher incidences of depression especially for those with uncontrolled seizures or other seizure syndromes. Tonic-clonic seizures did not show independent association with depression in the multivariate analysis indicating the likelihood that it was affected by other confounding factors.

Conclusion

Depression in patients with epilepsy is an important problem since it affects a significant number of patients treated with epilepsy. This study also shows that management of epilepsy in KATH can be improved.

Competing Interests

The author declares that there are no conflicts of interest to declare.

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