Factors associated with poor control of epilepsy at Kenyatta National hospital adult neurology clinic.

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A DISSERTATION SUBMITTED

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DECLARATION

I certify that this dissertation is my original work and has not been presented for a degree at any other university.

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DEDICATION

To Mativo's family

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LIST OF ABBREVIATIONS

KNH	Kenyatta National Hospital
EEG	Electroencephalograph
CT Scan	Computerized Tomographic Scan
MRI	Magnetic Resonance Imaging
CNS	Central Nervous System
FPIA	Fluorescence Polarisation Immunoassay
RV	Reaction Vessel
AED	Antiepileptic Drugs
Pheny	Phenytoin
Phenobarb	Phenobarbitone

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ABSTRACT

Background

Epilepsy is the most common neurological condition seen at KNH neurology clinic comprising of 16.6% of all neurologic diseases. Approximately 80% of epileptic patients achieve remission by the end of second year. It is a chronic illness with major psycho-socio-economic consequences. The mainstay of management remains chronic medication. Controlled epilepsy improves quality of life and motivates patients to seek medical care.

Poorly controlled epilepsy has been associated with higher rates of mortality, unemployment, and cognitive impairment. Several factors affecting control of epilepsy include drug adherence, biological factors, psychosocial factors, cultural factors and socio/economic factors. Few studies have been done locally on epilepsy especially on factors contributing to poor control of epilepsy.

Objectives

The main objective of the study was to examine the factors associated with poor control of adult epilepsy at KNH neurology clinic.

The specific objectives were;

1. To determine the prevalence of poor control among epilepsy patients attending the neurology clinic at KNH.
2. To determine the type of seizure among patients with epilepsy.
3. To determine the drug taking behavior among those epilepsy patients attending the neurology clinic at KNH.
4. To document the EEG characteristics among these patients.

5. To determine the random serum level of specified AED in a random sample of some well controlled and poorly controlled epileptic patients.
6. To document the CT scan characteristics among these patients.
7. To compare the above features among controlled and poorly controlled patients.

Design/Methods

The study design was a cross-sectional comparative study.

Study site

The study was undertaken at Kenyatta National Hospital adult neurology clinic.

Subjects

The study involved all patients with seizure disorders for more than 2 years in the KNH neurology clinic.

Study period

The study was undertaken between October 2003 and February 2004.

Results

Three hundred and sixty patients had seizures for more than 2 years and out of whom 180 were selected. The prevalence of poorly controlled epilepsy was found to be 40%. The mean age of the subjects was 28.73+/-11.96 years with a peak age group of 21-30 years and age range of 13 to 70 years. Poorly controlled patients were younger compared to well-controlled patients (27.53 years versus 29.93 years, P=0.028), and had longer duration of epilepsy (11.12 years versus 8.63 years, P=0.015). Although not statistically significant the poorly controlled group had more focal spikes and waves EEG pattern (40 versus 30, P=0.772), had more patients using alternative therapy (25 versus 15, P=0.0729), had poor drug adherence which was statistically significant (48 versus 24,

P<0.001), had missed drugs for longer duration in the last 3 months which was significant (12.81 versus 5.12 days, P=0.005). The number of AEDs, drug side effect profile, occupation, and education level were similar among the groups.

Conclusion

Poor control of epilepsy is still a major problem with a prevalence of 40%. The poor drug adherence is a major factor, which was associated with poor control of epilepsy due to financial reasons.

LITERATURE REVIEW

HISTORICAL ASPECTS:

Epilepsy is a disease of a thousand names. Over many years epilepsy has been given different names possibly because it is a common disease. Some of the names that were given to epilepsy were like lunatics, demons, the sacred disease, "seleniazetai" which describe people with epilepsy because they were thought to be affected by the moon's phases or by the moon god (Selene), falling sickness and so on[1]. Approximately 0.5-1% of all people suffer from epilepsy world wide[1]. The image which epilepsy, for example the grand mal attacks arouses among people is feelings of terror.

Special institutions for people with epilepsy in Germany were available until the second half of 19th century. They were put in prisons, lunatic asylums or former leprosaria if their families could not take care of them or seizures were uncontrollable[2],

In the Ayurvedic literature of Charaka Samhita (which has been dated to 400BC and is the oldest existing description of the complete Ayurvedic medical system), epilepsy is described as "apasmara" which means "loss of consciousness"[3]. Another ancient and detailed account of epilepsy is on a Babylonian tablet in the British Museum in London. This is a chapter from a Babylonian textbook of medicine comprising 40 tablets dating as far back as 2000BC. The tablet accurately records many of the different seizure types we recognize today[3].

The perception that epilepsy was a brain disorder did not begin to take root until the 18th and 19th Centuries A.D. The intervening 2,000 years were dominated by more supernatural views[4]. Throughout this time people with epilepsy were viewed with fear, suspicion and misunderstanding and were subjected to enormous social stigma[4]. People

with epilepsy were treated as outcasts and punished. Some, however, succeeded and became famous the world over. Among the great people who suffered from epilepsy are like Julius Caesar, Czar Peter the Great of Russia, Pope Pius IX, the writer Fedor Dostoevsky and the poet Lord Byron[3].

The foundation of our modern understanding of the derangement of function seen in epilepsy (pathophysiology) was also laid in the 19th Century with the work of Hughlings Jackson. In 1873 this London neurologist proposed that seizures were the result of sudden brief electro-chemical discharges in the brain. He also suggested that the character of the seizures depended on the location and function of the site of the discharges[5]. Working in Germany during the 1920s, Hans Berger, a psychiatrist, developed the human electroencephalograph (EEG - brainwaves'). Its important application from the 1930s onwards was in the field of epilepsy.

During the first half of this century the main drugs for treatment of epilepsy were phenobarbitone (first used in 1912) and phenytoin (first used in 1938) [6]. Since the 1960s, there has been an accelerating process of drug discoveries to manage epilepsy.

In the last few decades, greater attention has been paid to quality of life, for example, psychological and social issues, for people with epilepsy, although progress is slow and services are still poor. It is also the case that most of the advances in developed countries are of relevance but not available for the 80% of people with epilepsy who live in developing countries. Stigma is still the same in both developed and developing countries[3].

Of the 50 million people in the world with epilepsy, some 35 million have no access to appropriate treatment. This is either because services are non-existent or

because epilepsy is not viewed as a medical problem or a treatable brain disorder[3]. The incidence rate of epilepsy in developed countries is between 20 and 70 cases per 100000 and the prevalence rate of active epilepsy ranges between 4 and 10 per 1000[7]. The incidence and prevalence rates in developing countries are claimed to be higher than developed countries[7]. The prevalence of seizures is higher among populations living in poor socio-economic state[8].

The following is a summary of epileptic patients seen at KNH neurology clinic from medical records.

YEAR	NEW	OLD	TOTAL
2000	571	1760	2331
2001	616	2366	2982

CLINICAL PICTURE

Epilepsy is the name of occasional sudden, excessive rapid and local discharges of gray matter[5]. Epileptic seizure can be defined as an intermittent, stereotyped, disturbance of consciousness, behavior, emotion, motor function or sensation that on clinical grounds is believed to result from cortical neuronal discharges. It can also be defined as a condition in which seizures recur spontaneously.

Spike and sharp wave is the E.E.G hallmark of interictal recording in patients with epilepsy. In some studies of patients with epilepsy, an initial E.E.G revealed spikes in 55% and, if E.E.Gs were repeated regularly, only 8% of patients with epilepsy continued to have records that never showed sharp waves or spikes in the E.E.G[9, 10]. Such activity appears to be due to hypersynchronisation of electrical activity within an abnormal pool of neurons, and they are rarely seen in the E.E.Gs of non-epileptic

patients. Less than 2% of the general population has interictal epileptiform EEG activity hence abnormal EEG is not definitive of epilepsy.

There is an increased mortality ratio for epilepsy persons of between 2-3 times the expected[11]. The greatest mortality seems to occur in early years of life and to be more obvious in men[12]. Mortality is highest for patients with tonic-clonic seizures and seizures that recur frequently. The risk is higher for patients with symptomatic epilepsy than for those with idiopathic condition[11]. Much of the excess mortality seems to be associated with the underlying etiology of the epilepsy.

The classification given below is modified from the Commission on Classification and Terminology of the International League Against Epilepsy (Appendix I).

There are many causes of epilepsy. Most cases of epilepsy are idiopathic (approximately 67%) and usually begin by the age of between 5 years and 20 years, have no neurological abnormalities and often have family history. The causes in the rest of epilepsy are metabolic abnormalities, CNS infections, head trauma, anoxia, and toxins, intracranial space occupying lesions, circulatory disturbances like stroke, and cerebral edema from any cause, congenital causes, and degenerative diseases. Slightly over half the seizures in adults are complex partial types, of which 80% originate in the temporal lobe of the brain[13].

Local data on epilepsy is scanty. A retrospective study done in KNH (1992) showed that neurological diseases constituted 7.5% of all medical conditions seen in medical wards[14]. Epilepsy constituted 16.6% of neurological diseases and was second most common after meningitis in adult population[14]. Another study done earlier showed epilepsy was fourth commonest after congenital malformations, infections, and space-

occupying lesions among Kenyan children[15]. In slightly over 50% of the cases of epilepsy in KNH, the cause was unknown. Trauma due to road traffic accidents and infection were second and third commonest cause of epilepsy respectively[16].

A community survey done in 1991 in Nakuru district showed that majority of patients had never had previous contact with a formal medical system. The mean age of seizure onset was 14 years with mean duration of seizures of 7 years[17]. In 77% of the cases, no aetiology was established. Most cases had a substantial number of seizures during the course of their condition and only about a third of the patients had less than one seizure a month in the previous year. Only 26% had ever had previous anti-epileptic drug treatment. The prevalence of epilepsy in Nakuru district was 18 per 1000 population[17].

Epilepsy is a chronic illness and treatment is often life long. Noncompliance with medication regimens is widespread.[18] Between 30% and 40% of epileptic patients appear to be noncompliant with their drug regimen (the range is 20% to 75%)[19]. In a survey of black epileptics in South Africa[20], an overall non-compliance rate of 50% was found. Similarly it has been shown that 30% of African epileptic children did not take their tablets at all using serum drug assays [21].

Compliance is defined as the "readiness on the part of the patient to cooperate with diagnostic and therapeutic measures''[22]. Noncompliance may be defined as not taking the correct dosage of medicine (too much or too little), failing to follow dosing schedules, not taking medication for the duration specified, or taking other, non-recommended medications[23]. Failure to comply with treatment regimens leads to increased seizure recurrence. Poorly controlled seizures increase the likelihood of

hospital admission, increased frequency of injuries, loss of employment and loss of workdays[23, 24].

Leppik broadly defines compliance in terms of three dimensions: type of behavior, extent of compliance, and degree of intentionality[18]. The type of behavior includes medication ingestion, keeping clinic appointments, and filling prescriptions properly. The extent of compliance ranges from the person who takes every prescribed dose precisely as directed, to the one who never does. Lastly the degree, to which patients intend to comply with the regimen, is divided into two categories: patient-controlled (rational or irrational behaviors) and structural like loss of memory and limited access to medication[18].

Reasons for noncompliance are often patient-specific, multifaceted, and change over time[25]. Noncompliance can be due to limited access to medications, complex dosing regimens[23, 24], poor patient education[23, 24,26], medical factors such as the effect of co-morbid conditions and unwanted adverse side effects, and psychosocial factors such as family support[27-29], and use of alternative therapy like prayers and herbs[30].(Appendix V).

In a study done at KNH in 1984, Lisk showed that 70% of literate patients were drug compliant as compared to 44% who were not. It also showed that seizure control did not relate to compliance. Patients on single medication had a higher degree of compliance[31]. In this study, 60.9% were controlled and 39.1% uncontrolled[31].

Approximately 1.5-5.0% of the population may have at least a seizure in their lifetime. Approximately 60% of epileptics achieve remission after the first year; 15% achieve control at a later date, but in 25% seizures resist control and become intractable[32]. At least 2 years are required of medical treatment of epilepsy to ensure that several major

anti-epileptic drugs have been pushed to their therapeutic limits and that the likelihood of spontaneous improvement has been diminished before surgical therapy is considered for refractory epilepsy[33].

Ineffective treatment delayed or lack of access to high-quality, specialized care, and the severity of the underlying neurological disorder are all possible contributors to the development of hard to control seizures.

Epileptic patients who respond early to drug therapy have the best long-term outcome especially those who respond within the first year of treatment.[33] In contrast, those who do not respond within 2 years may be candidates for brain surgery[34]. In spite of medical therapy, seizures persist in approximately 20% of patients with primary generalized epilepsy and 35% of patients with partial epilepsy[35-37].

Epilepsy is refractory when seizures are so frequent or severe that they limit the patient's ability to live life fully according to his or her own wishes or necessitate the use of medications that, although effective, produce adverse effects. Potential causes of poorly controlled seizures include incorrect classification of the seizures, inadequate antiepileptic drugs (AED) therapy, competing epileptogenic drugs such as phenothiazines, and biologically intractable seizures[38]. Patients with intractable epilepsy who meet certain diagnostic standards may benefit from brain surgery[39] or vagal stimulation[40] or ketogenic diet in children[41].

Refractory epilepsy can be confused with conditions such as syncope[42], migraine[43], and non-epileptic seizures[44, 45] among others. Due to this scenario one has to take a good history and physical examination although they can also occur together with epilepsy[42-45]. Around 15% of patients diagnosed to have refractory epilepsy will not have

epilepsy while 10-20% of those with epilepsy may not have received appropriate AEDs[46]. Magnetic resonance Imaging (MRI) should be obtained to rule out a structural lesion in this group of patients[47].

Drug noncompliance and lifestyle factors such as sleep deprivation, emotional stress, menstrual cycle, flickering lights and other sensory stimuli, alcohol use or withdrawal, and illness can trigger recurrence of epilepsy[48, 49].

Most physicians will stop medication after 2-4years of a seizure free period so long as the cause has been removed if known.

PHARMACOLOGY OF SOME ANTIEPILEPTICS

Currently available antiepileptic drugs appear to act primarily by blocking the initiation or spread of seizures. The mechanisms are diverse and some established ones are given below. Phenytoin, carbamazepine, topiramate, and zonisamide act through inhibition of sodium dependent action potentials in a frequency dependent manner. Phenytoin also inhibits voltage gated calcium channels. Lamotrigine decrease glutamate release while benzodiazepines and barbiturates potentiate GABA receptor function. Increase in the availability of GABA is the mechanism of valproic acid, gabapentin and tiagabine. Ethosuximide and valproic acid probably act by inhibiting T-type calcium channels in thalamic neuron[50].

The drugs commonly used in our set up for control of seizures are carbamazepine, phenytoin, valproic acid and phenorbarbitone. Phenytoin has limited aqueous solubility hence when taken orally its absorption is slow, sometimes variable and occasionally incomplete. Due to slow absorption, chronic use blunts the fluctuation of drug serum

concentration between doses. Phenytoin levels are routinely monitored because of its narrow therapeutic range and non-linear kinetics[50].

Phenobarbitone has a long half- life hence it takes weeks for plasma concentration to reach plateau level. The absorption of carbamazepine is slow and erratic and the peak plasma levels reach after 4-8hours although it can extend to 24hours. Valproic acid is well absorbed in the gut and has a half-life of 12-15hours. Carbamazepine and phenobarbitone levels assessment can be useful in certain cases where control is inadequate[50].

The monitoring of serum levels of the other antiepileptic drugs is of limited clinical value[51]. Drug monitoring is important in the process of drug treatment in order to optimize efficacy, analyze compliance, and avoid and identify toxicity[52].

Justification of the study

Epilepsy is the most common neurological condition seen at KNH neurology clinic. It is a chronic illness with major psychosocial and economic consequences.

Epilepsy is amenable to treatment. Approximately 80% of patients achieve remission by the end of second year. Controlled epilepsy improves quality of life and motivates patients to seek medical care, whereas poorly controlled epilepsy has been associated with higher rates of mortality, unemployment, and cognitive impairment.

The mainstay of management remains chronic medication. Adherence to chronic medication is often poor due to various factors including fatigue of taking drugs, drugs' side effects, unavailability, inaccessibility, and financial constraints. There are different preparations of the same AED i.e. different brands in the market, which could have different drug levels and half-life and this can affect epilepsy control. From unpublished data, there are many patients who are poorly controlled followed up at KNH neurology clinic. Local studies on factors related to poor control are scanty hence the need for the study.

The study was therefore aimed at assessing major factors that contribute to poor control. The result of this study will not only add to the research database, but also contribute to the strategy on how to deal with poorly controlled patients.

OBJECTIVES

Main objective

To study the factors associated with poor control of adult epilepsy at KNH neurology clinic.

Specific objectives

1. To determine the prevalence of poor control among epilepsy patients attending KNH neurology clinic.
2. To determine the type of seizure among patients with epilepsy.
3. To determine the drug taking behavior among those epilepsy patients attending KNH neurology clinic.
4. To document the EEG characteristics among these patients.
5. To determine the random serum level of specified AEDs in a random sample of some well controlled and poorly controlled epileptic patients.
6. To document the CT scan characteristics among some of these patients.
7. To compare the above features among those controlled and those poorly controlled patients.

PATIENTS AND METHODS

1. STUDY DESIGN

The study was a comparative cross-sectional study.

2. STUDY SITE

The study was undertaken at KNH adult neurology clinic.

3. SUBJECTS

The study involved all patients with seizure disorder for at least 2 years in the KNH neurology clinic.

4. SAMPLING

Consecutive random selection was used to recruit all patients until the required number was reached so long as they fulfilled the inclusion criteria.

5. INCLUSION CRITERIA

- Patient should have had epilepsy for at least two years.
- Written informed consent by the patients or parent or guardian if the patient was less than 18 years old.
- Patient had to have an EEG report.

6. EXCLUSION CRITERIA

- Failure to give a written informed consent.

7. SAMPLE SIZE

The minimum sample size was 90 patients with poorly controlled epilepsy with a similar number of epilepsy patients who were well controlled. The formula used to calculate the sample size is the following:

$n=[(Z1\text{-}a/2)^2 p(1\text{-}p)]/d^2$

Where n = sample size

Z = normal standard deviation

P =estimated patients with uncontrolled epilepsy (39%)

d = desired degree of precision or accuracy (10%)

(Z1-a/2) =1.96, corresponding to a significance level of 0.05.

8. MATERIALS AND METHODS

8.1. PATIENT

All the records of patients scheduled to attend the neurology clinic the next day and known to have seizure disorders were scrutinized. Files of patients who had been followed up for epilepsy for two or more years were selected.

The study was undertaken in two parts. For the purpose of prevalence, all consecutive patients were recruited, while for the second part i.e. objectives 2 to 7, only patients who had an EEG were recruited. From the patient's records and collaborative history during the interview, seizures were classified according to International League Against Epilepsy (ILAE) 1989. Patients who were recruited were interviewed to determine if they were poorly controlled or well controlled. Poor control was defined as more than one seizure in the last six months.[31] Recruitment of patients continued until the required number of 90 well-controlled patients, with a similar number of poorly controlled patients was reached. The selected patients or their parents/guardian in case of minors gave a written informed consent before they could participate in the study.

1. All the selected patients were counselled about details of the study. A detailed demographic data was obtained and recorded for those selected. (See questionnaire appendix-I)

3. The interview included seizure characteristics, alcohol use, head trauma and AEDs taking behaviour and current medications.
4. From the files, documentation of EEG findings was done for those patients who had already done an EEG. Where an EEG was not available, it was done before the patient could be included in the study.
5. From the files, documentation of CT scan findings of the head was only done on those patients who had already done one as part of evaluation for their seizures. It was not ascertained the reason(s) for having done the CT scan. The analysis was therefore done in only those documented CT scans.
6. Blood from consecutive randomly selected poorly controlled patients and well-controlled patients was obtained for random serum drug levels of selected anticonvulsant drugs, which are commonly used.

8.2. LABORATORY METHODS

The random serum drug levels were analysed using Abbott AxSYM Immunoassay Analyser Machine. The soft ware used was of 1993. The AxSYM Phenobarbital, Phenytoin, Carbamazepine, Valproic acid assays utilizes Fluorescence Polarization Immunoassay (FPIA) technology. Controls were done using AxSYM Phenobarbital, Phenytoin, Carbamazepine, Valproic acid Controls. The full procedure used for the serum drug analysis is in appendix V.

9. DATA ANALYSIS

The data from the questionnaire was coded before entering it into a computer using SPSS 10.0 software. Cleaning and verification was done before analysis using SPSS 10.0 and Epi Info 2002 softwares. Means, range, and standard deviation were used to summarise the data. It is presented using tables, histogram, bar charts and pie charts. Association was examined using chi square test for categorical data and a P value of 0.05 was taken as significant. For continuous variables, the student t-test was used to determine significance.

10. ETHICAL CONSIDERATIONS

Informed written consent was taken from the patient recruited (appendix II). For the minors (below 18 years), informed consent was taken from the parent or guardian (appendix III).

Permission to do the study was given by KNH scientific and ethical review committee. The information obtained was confidential and only used for purpose intended. Feedback to the patients was given where applicable.

RESULTS

The data was collected between October 2003 and February 2004 at Kenyatta National Hospital Adult Neurology Clinic. The study was in two parts. In order to get prevalence of poor control, all patients who had seizures for more than 2 years were recruited. Out of 360 case files recruited, 144 cases were poorly controlled giving a prevalence of 40%.

For the second part of the study, only 90 patients who were poorly controlled had full documentation and an EEG report and were recruited for the second part of the study. A similar number of consecutive patients who were well controlled were recruited. (See figure 1)

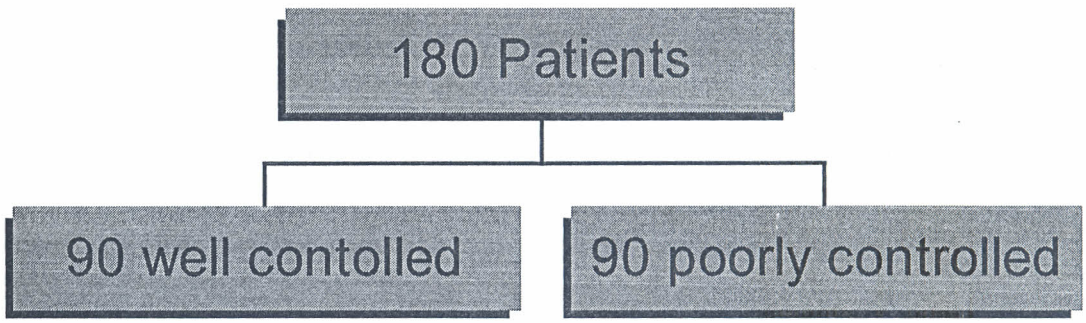


Figure 1. Flow chart of the epileptic patients recruited in the study and their categorization.

COMPARISON BETWEEN THE CHARACTERISTICS OF CONTROLLED AND POORLY CONTROLLED PATIENTS

The mean age of the total group of patients was 28.733+/-11.96 years with a range of 13-70 years. The peak age group was 21-30 years in both controlled and poorly controlled patients. The mean age for male patients was 29.29+/-11.70 years with a range of 13 to 70 years while for female patients was 28.00+/-12.32 years with a range of 13 to 70 years. (See figure 2.)

The mean age of well-controlled patients was 29.93+/-13.47 years with a range of 13 to 70 years while for poorly controlled patients was 27.53+/-10.15 years with a range of 14 to 53 years. The poorly controlled had a significantly higher mean age than well controlled at P value of 0.028.

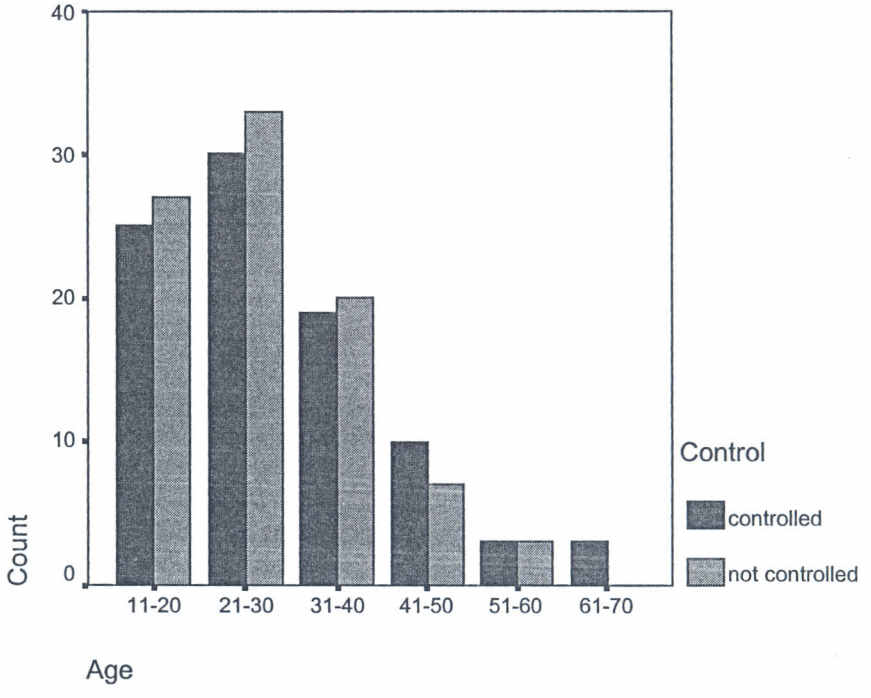
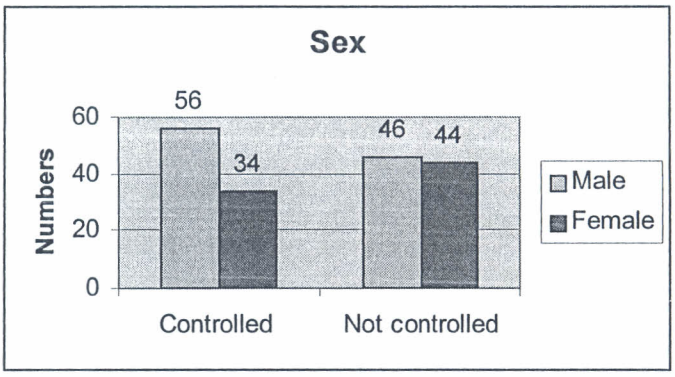


Figure 2. Age distribution of well controlled and poorly controlled patients at the KNH neurology clinic.

One hundred and two (57%) patients were male and 78 (43%) females with a ratio of 1.3:1. There was no statistical significant difference in the gender distribution of controlled and poorly controlled at a P value of 0.088. (See figure 3)



P= 0.088

Figure 3. Gender distribution of well controlled and poorly controlled patients

Fifty percent of the patients were from Nairobi province, 29% from central *province, 14% from Eastern province* and the others from the rest of the country. (See figure 4 below)

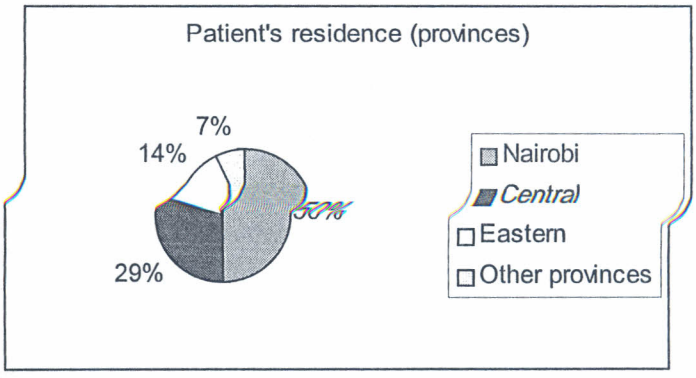


Figure 4. Regional distribution of the patients involved in the study.

The majority of the patients were unemployed 63 (35%) and with students accounting for 26% of cases. Sixty three percent of unemployed patients were poorly controlled as compared to 37% of unemployed patients who are well controlled as shown in table 1.

Occupation	Controlled (%)	Not controlled (%)	Total
Unemployed	23 (37%)	40 (63%)	63
Student	28 (61%)	18 (39%)	46
Formal employment	16 (48%)	17 (52%)	33
Informal sector	15 (75%)	5 (25%)	20
Business person	8 (44%)	10 (56%)	18
Total	**90**	**90**	**180**

Table 1. Occupation distribution of patients with epilepsy

One hundred and seventy seven (98%) patients had at least primary school education. Patients who had attained a minimum of secondary level of education were 108 (60%). The level of education among the groups was fairly similar between the two groups. (See figure 5)

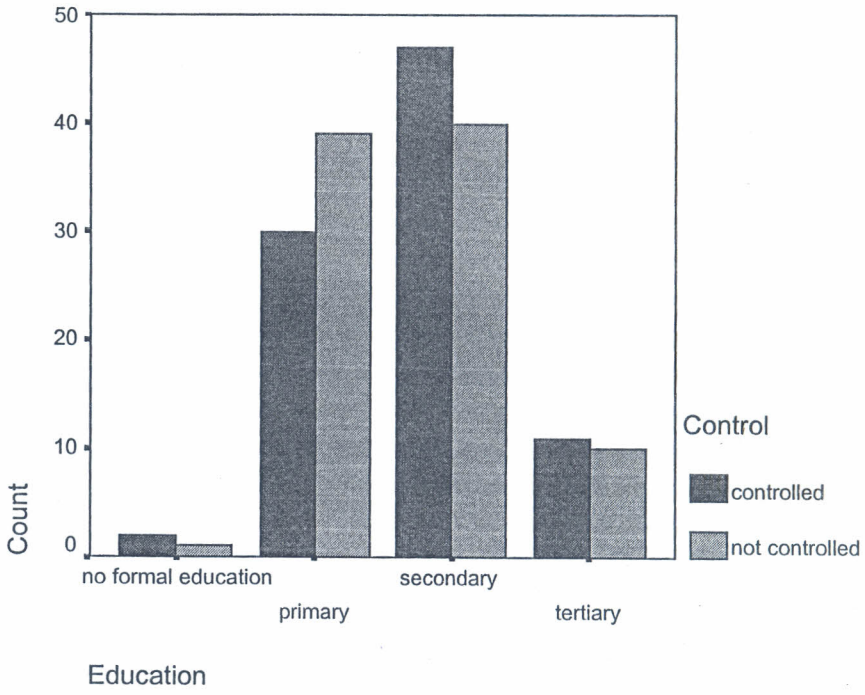


Figure 5. Education level of patients who were well controlled and poorly controlled.

The mean duration of seizures among the patients who had well-controlled epilepsy was 8.63+/-8.25 years with a range of 2 to 40 years while it was 11.12+/- 9.77 years with a range of 2 to 40 years for the poorly controlled and this was statistically significant with a P value of 0.015.

Approximately 77% of the total group claimed not to know the perceived cause (aetiology) of their illness. Eighty three percent of patients who were poorly controlled said they did not know the perceived cause of their illness as compared to 70% well-controlled patients at significant P value of 0.034. Most patients thought epilepsy was due to stress and head injuries. (See table 2)

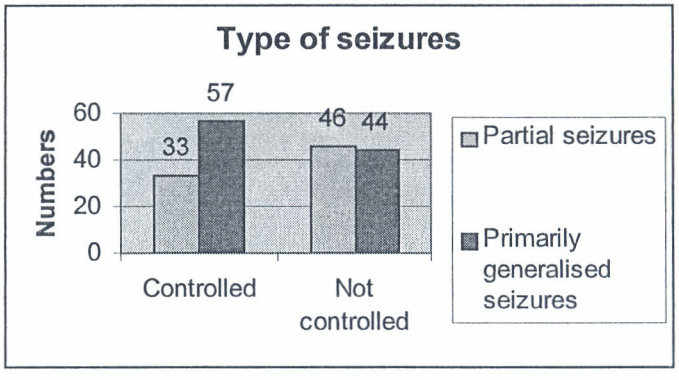
Perceived cause	**Number (%)**
Don't Know	138 (77%)
Stress	18 (10%)
Head injury	17 (09%)
Febrile illness	4 (02%)
Inheritance	2 (01%)
CVA	1 (01%)
Total	**180 (100%)**

Table 2. The perceived cause of their illness by the study patients

There were only 33 (18%) patients who had history of head injury. Twenty-one, (64%) patients with history of head injury were well controlled while 12 (36%) were poorly controlled. The difference between the groups was not statistically significant with a P value of 0.061.

Twenty-nine (16%) patients of the total group had family history of epilepsy, among them, 16 (55%) patients were poorly controlled and the rest were well controlled. It was however found not to be statistically significant with a P value of 0.343.

One hundred and one (56%) patients were classified to have primarily generalized seizures and 79 (44%) partial seizures. More patients with partial seizures were poorly controlled as compared to well controlled at 46 (58%) and 33 (42%) respectively. Fifty-seven, (63%) patients who were controlled had primarily generalized seizures as compared to 44 (49%) who were poorly controlled. This difference was not statistically significant with a P value of 0.050. (See figure 6)



P= 0.050

Figure 6. The type of seizures among well controlled and poorly controlled patients.

Most patients 46% (84) had normal EEG, 14% (26) and 40% (70) had generalized epileptiform spikes and focal spikes and waves respectively. Of the patients who were poorly controlled, 54 (56%) had abnormal EEG as compared to patients who were well controlled with 42 (44%) having abnormal EEG with a statistically not significant P value of 0.073. (See figure 7)

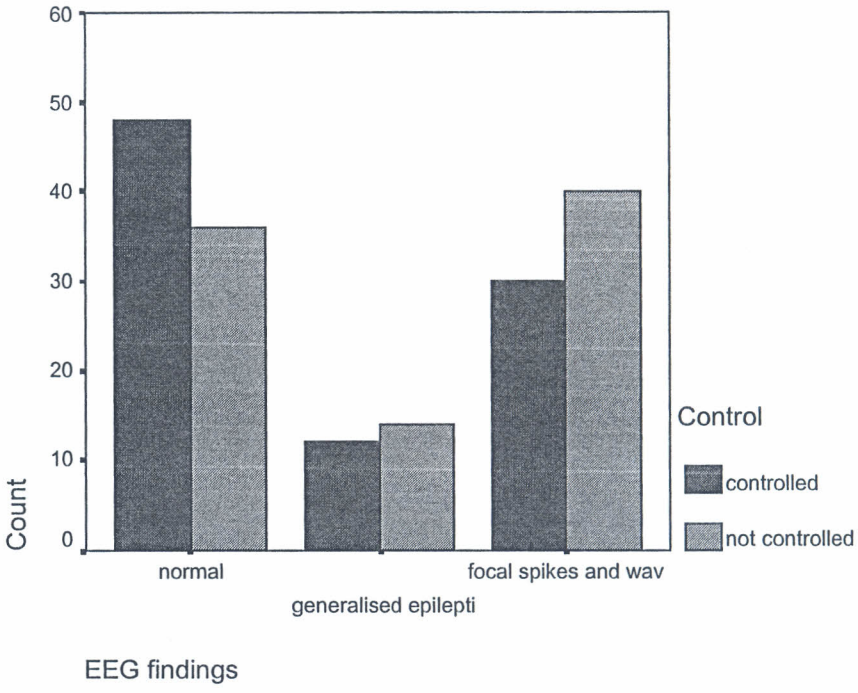
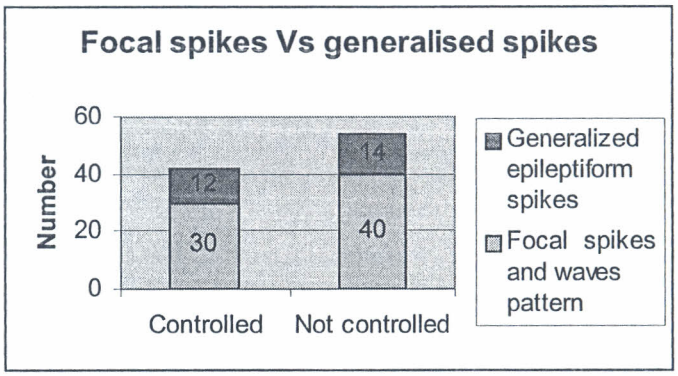


Figure 7. EEG findings among poorly controlled and well-controlled patients.

Patients were further subdivided into those with generalized epileptifom spikes EEG and focal spikes and waves EEG. Among patients who were poorly controlled, 40 (44%) had focal spikes and waves EEG pattern while14 (16%) patients had generalized epileptiform spikes pattern. Thirty patients (33%) who were well controlled had their EEGs reported as focal spikes and waves pattern and further 12 (13%) patients had EEG with generalized epileptiform spikes. This was not statistically significant among the groups. (See figure 8)



P=0.772

Figure 8. Comparison between focal spikes and waves and generalized spikes among poorly controlled patients and well-controlled patients.

Forty-nine patients (27%) among the total group had CT scan of the head. Out of those CT scans, 37 (76%) were normal and 12 (24%) scans had abnormal findings. This was a coincidental observation that 7 patients who were poorly controlled had abnormal CT scan findings as compared to 5 who were well controlled. The number was too small to carry out any statistical test.

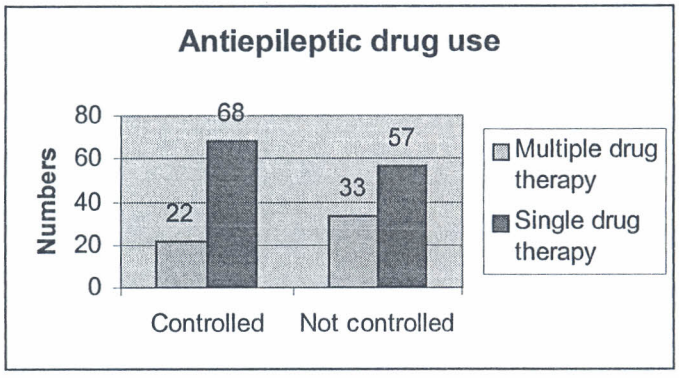
Brain infarct was the commonest pathology seen among the patients done CT scan and the rest as shown in the table 3.

Reported findings	**Total (%)**
Brain infarcts	7 (58%)
Brain atrophy	3 (25%)
Both infarct & atrophy	1 (8.5%)
Depressed fracture	1 (8.5%)

Table 3. Summary of the abnormalities found in the CT scan

One hundred and twenty five (70%) patients were on single anti-epileptic drug therapy (monotherapy) while the rest were on multiple therapies. Patients who were well controlled tended to be on monotherapy unlike poorly controlled whereas the inverse for

use of multiple therapies was true though it was not statistically significant with P value of 0.075 as shown in figure 9.



P= 0.075

Figure 9. Use of antiepileptic drugs by controlled and poorly controlled patients

Among patients on monotherapy, 76 (61%) were on carbamazepine, 36 (29%) on phenytoin, 7 (6%) on phenobarbitone and the rest on sodium valproic acid as shown in table 4.

Drug	**Controlled**	**Not controlled**	**Total (%)**
Carbamazepine	36	40	76 (61%)
Phenytoin	27	9	36 (29%)
Phenobarbitone	4	3	7 (6%)
Valproic acid	1	5	6 (4%)
Total	**68**	**57**	**125 (100%)**

Table 4. Distribution of monotherapy regimen used by the patients.

Carbamazepine and phenytoin were the most used combination therapy among all the total patients accounting for 33%, followed by carbamazepine with phenobarbitone at 27%. The other combination therapies are as shown in the table 5.

Drugs	Total (%)
Carbamazepine/Phenytoin	18 (33%)
Carbamazepine/Phenobarbitone	15 (27%)
Phenytoin/Phenobarbitone	11 (20%)
Carbamazepine /Pheny/Phenobarb.	5 (9%)
Carbamaz/Valproic	4 (7%)
Valproic/Phenobarbitone	1 (2%)
Carbamazepine/Valproic/Phenobarb.	1 (2%)
Total	**55 (100%)**

Table 5. Combination regimens used by the patients.

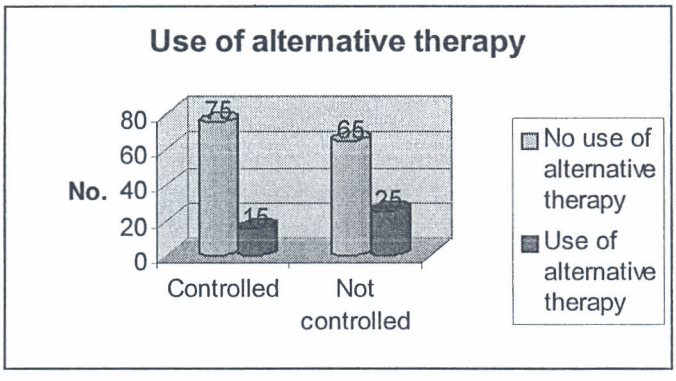
Only 28 patients who comprise 15.6% of the total sample size were using medications for other ailment concurrently. Most of them were on anti-hypertensives or anti-psychotics or folate. As a coincidental observation, 6 patients who were not controlled were on anti-psychotics as compared to one who was well controlled and the number of patients was too small to subject it to statistical test. (See table 6 below)

Other medications	Total (%)
Antihypertensives	8 (29%)
Antiasthmatics	2 (7%)
Antipsychotics	7 (25%)
Folate	7 (25%)
Others	4 (14%)
Total	**28 (100%)**

Table 6. Other concurrent medications used by the patients with epilepsy.

Forty (22%) of the total group was on alternative therapies for epilepsy. There was an increase in the use of alternative methods among the poorly controlled patients

with 63% using alternative methods as compared to 37% of the well controlled. This difference did not reach statistical significance at P value of 0.073. (See figure 10)



P= 0.0729

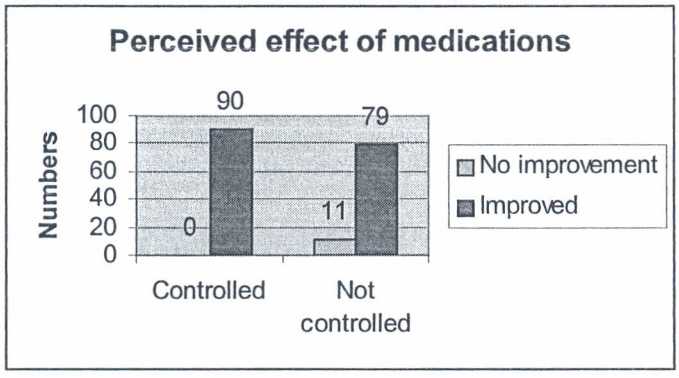
Figure 10. The use of alternative therapy among well-controlled patients and those who were poorly controlled.

Out of the patients who used alternative therapy, 29 (73%) used herbs and 11 (27%) used prayers. (See table 7)

Alternative therapy used	**Total (%)**
Herbs	29 (73%)
Prayers	11 (27%)
Total	**40 (100%)**

Table 7. Shows the form of alternative therapy used by the patients.

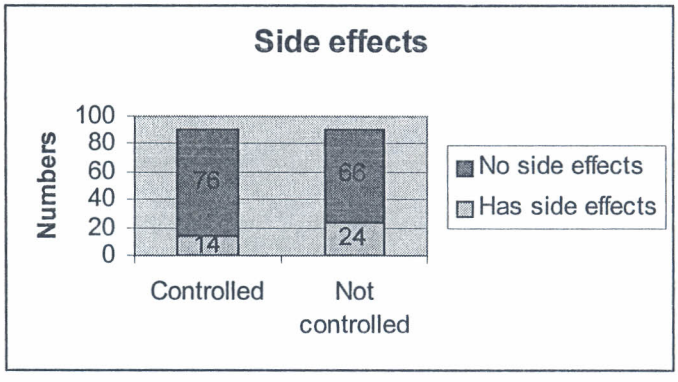
Over 93% of patients in both groups reported marked improvement on the number of seizure attacks. Eleven (7%) poorly controlled patients reported no improvement on treatment as compared to none who were well controlled. It was found to be statistically significant between both groups. (See figure 11)



P= 0.003

Figure 11. The effects the patient had after being on treatment with antiepileptic drugs.

Thirty-eight, (22%) patients had experienced side effects during their cause of treatment. Fourteen (37%) patients of those who experienced side effects were well controlled while the rest were poorly controlled. The comparison was not statistically significant among the groups as shown in figure 12.



P= 0.0677

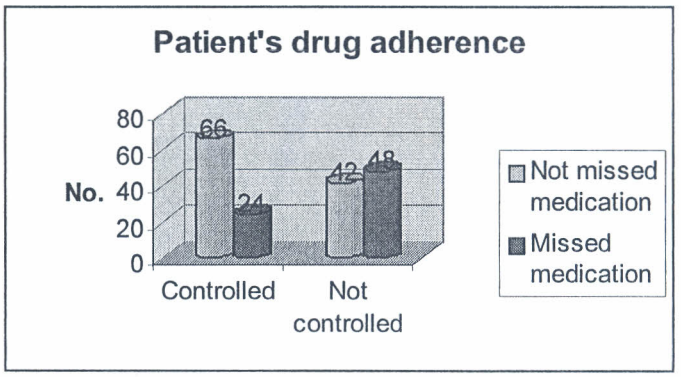
Figure 12. Frequency of side effects experienced by controlled and poorly controlled patients.

Sedation was the commonest side effect experienced by 28 (73%) of patients followed by ataxia/incoordination with 7 (18%) of patients. (See table 8)

Side effects	Total (%)
Sedation	28 (73%)
Ataxia/In coordination	7 (18%)
Skin lesion	1 (3%)
Anorexia	1 (3%)
Gum hypertrophy	1 (3%)
Total	**38 (100%)**

Table 8. Shows the various side effects experienced by the patients.

Seventy-two patients (40%) of the total group were not adhering to their antiepileptic medication. Among the poorly controlled patients, 48 (67%) were not adhering to their antiepileptic treatment as compared to 24 (33%) well-controlled patients. This was found to be statistically significant with a P value <0.001. (See figure 13)

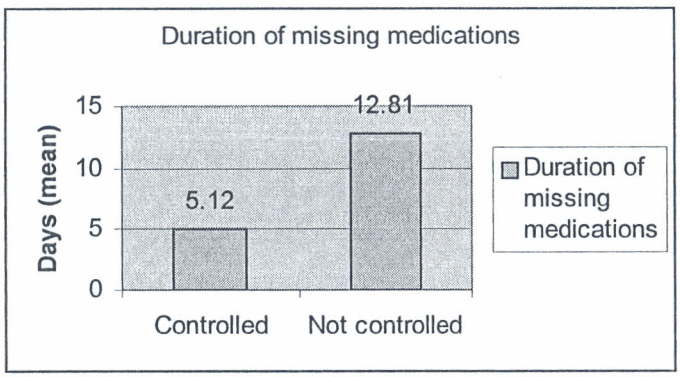


P< 0.001

Figure 13. The number of patients who were not adherent to their antiepileptic medications both poorly controlled and well controlled patients.

The mean duration of days patients who were well controlled missed medication was 5.12+/- 6.51 days with a range of 1 to 30 days, while for those who were poorly controlled the mean duration was 12.81+/-23.41days with a range of 1 to 120 days. This difference was found to be statistically significant among the groups. Patients who were

poorly controlled missed to take their anti-epileptic medication for a longer duration in the preceding 3 months as compared to the well-controlled patients. (See figure 14)



P= 0.005

Figure 14. The number of days controlled and poorly controlled missed their medication in the last 3 months

The reasons for non-adherence on medication are as shown in table 9. Financial difficulties and forgetfulness were the main reasons for poor drug compliance.

Reason for non-adherence	**Total**	**(%)**
Financial difficulties	25	(35%)
Just forgetting	17	(23%)
Unavailability	10	(14%)
Inaccessibility	7	(10%)
Side effects	3	(04%)
Others	10	(14%)
Total	**72**	**(100%)**

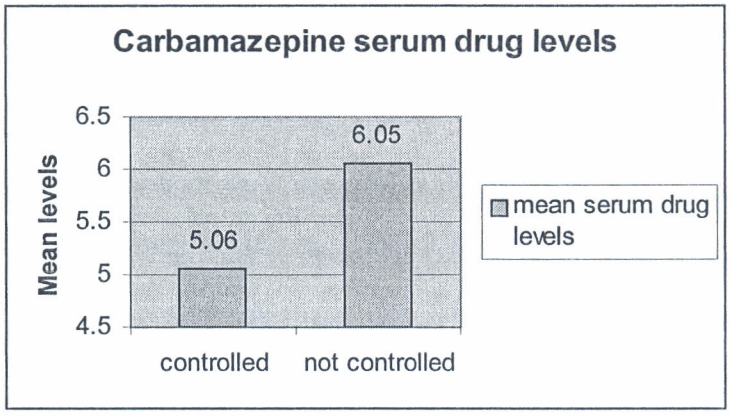
Table 9. Reasons for missing drugs among all the patients with seizures.

Sixty-one percent of all the random serum drug levels were sub therapeutic level. At least 55% of random serum carbamazepine drug levels were sub therapeutic, while phenytoin was 67%, phenobarbitone was 40% and lastly sodium valproic was 75%.

Carbamazepine was the most widely used anti-epileptic drug. The mean 24-hour dose of carbamazepine in patients who were well controlled was 416.35+/-278.25mgs

with a range of 50mgs to 1400mgs, while in poorly controlled was 660+/-340.86mgs with a range of 100mgs to 1600mgs. The comparison between the two groups was not statistically significant with a P value of 0.104.

The mean random serum carbamazepine drug levels of patients who were well controlled were 5.06+/-2.9ug/ml with a range of 0.00ug/ml to 9.75ug/ml while for those who were poorly controlled were 6.06+/-4.67ug/ml with a range of 0.05ug/ml to 16.42ug/ml. The difference between the two was statistically significant with a P value of 0.007. (See figure 15)



P= 0.007

Figure 15. The random serum carbamazepine levels among controlled and poorly controlled patients.

Phenytoin was the second most commonly used anti-epileptic drug. The mean 24-hour phenytoin dose used by patients who were poorly controlled was 274.14+/-127.21mgs with a range of 50mgs to 600mgs, while for those well controlled was 243.13+/-109.34mgs with a range of 25mgs to 600mgs. This difference was not statistically significant between the two groups with a P value of 0.375.

The mean random serum phenytoin drug levels done to patients who were well controlled were 7.82+/-8.12ug/ml with a range of 0.00ug/ml to 35.59ug/ml, while for patients who were poorly controlled was 5.65+/-4.96ug/ml with a range of 0.37ug/ml to

13.22ug/ml. The difference among the groups was not statistically significant with a P value of 0.502. (See figure 16)

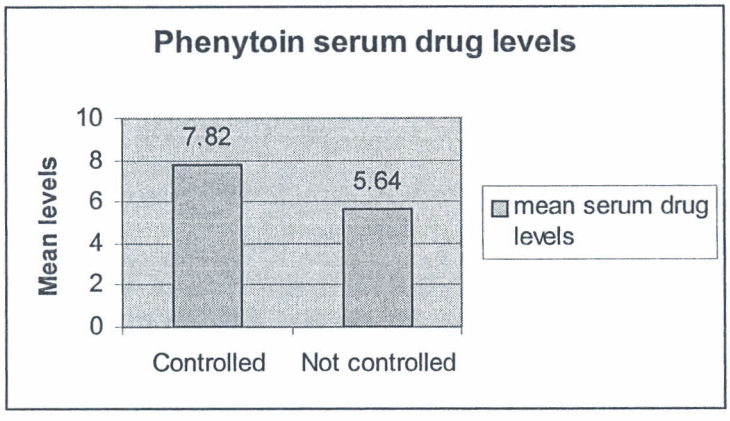
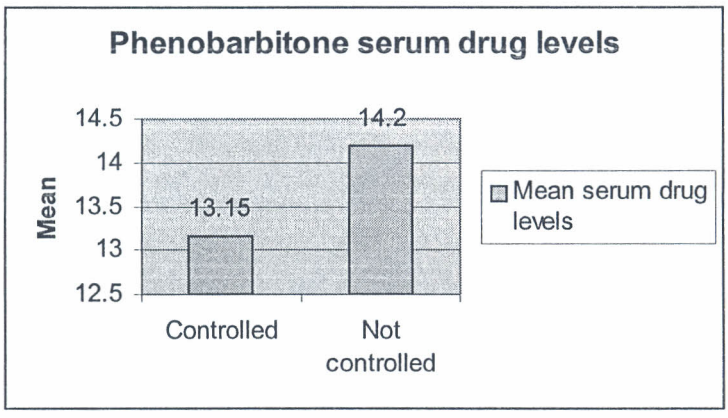


Figure 16. The random serum phenytoin levels among controlled and poorly controlled patients.

Phenobarbitone was the third most frequently used anti-epileptic drug. The mean 24-hour phenobarbitone dose used by patients who were well controlled was 74.21+/-37.91mgs with a range of 30mgs to 180mgs, while for those who were poorly controlled was 89.38+/-39.19mgs with a range of 45mgs to 180mgs. The P value among the groups was 0.656 and was found not to be statistically significant.

The random serum phenobarbitone drug levels among patients who were poorly controlled were 14.2+/-12.33ug/ml with a range of 0.10ug/ml to 36.32ug/ml, while for those who were well controlled was 13.15+/-9.41ug/ml with a range of 0.00ug/ml to 34.62ug/ml. The difference among the groups was not statistically significant as shown in figure 17.



P= 0.334

Figure 17. The random serum phenobarbitone levels among controlled and poorly controlled patients.

Sodium valproic acid was the least used anti-epileptic drug. The mean 24-hour dose of the patients who were well controlled was 500+/-141.42mgs with a range of 400mgs to 600mgs, while for those who were poorly controlled were 863.63+/-510.44mgs with a range of 300mgs to 1800mgs. It was found not to be statistically significant with a P value of 0.098.

The mean random serum sodium valproic drug levels were only done on 4 patients who were poorly controlled and were 18.75ug/ml with a range of 0.00ug/ml to 46.54ug/ml. No patient who was well controlled was done random serum sodium valproic acid drug levels hence we cannot calculate the P value.

DISCUSSION

Epilepsy is a chronic condition, which requires long-term medications. The outcome of the control solely depends on long-term adherence to therapy. Only patients with EEGs were included in the study. This could have left patients who were poorly controlled who could not afford doing an EEG due to financial reasons, and patients who were well controlled and therefore did not have to do one leading to a selection bias. With the known limitations of EEG, which was the primary entry point, being the first study of its kind in our set up, the study findings are still valid and important in addressing the study question of control of epilepsy.

This study found that 40% of the patients attending the neurology clinic had poor control of seizures. In 1984, Lisk did a similar study in 72 patients in the neurology clinic and found that 39.1% of the patients were poorly controlled. This study used a questionnaire as the instrument to qualify seizure control. Drug levels were not used to assess drug adherence[31]. This study done 20 years later shows no change in the prevalence of control despite the introduction of more potent anticonvulsants. The poverty level, which contributes to major issue in control, still remains. It is unfortunate that this situation continues despite advances in medical practice.

Studies in western countries have shown very high rate of control reaching up to 75% and over at 2 years[32, 33]. The reasons for this achievement are not clear. Seizure type like partial seizures tend to be more resistant to control[53]. In our study 44% of the total number of cases had partial seizures. We further found that partial seizures were associated with poor control. This has also been shown in several studies in the past where partial seizures are associated with recurrence of seizures.

In most studies in developing countries primarily generalized seizures are considered much more common than partial seizures. In Indian subcontinent studies, primarily generalized seizures accounted for 45-86%, while partial seizures with or without generalization formed 11-55%[54]. In Tanzania the prevalence of primarily generalized seizures was 58%[55]. In contrast, studies from developed countries show that partial seizures accounted for more than 50% of cases[54]. There has been argument on this with most researchers believing that generalized seizure appear to be more prevalent due to their presentation. Our study however did find generalized seizure to be more prevalent among the patients.

Fifty four percent of the total study cases had epileptiform EEG pattern, among these, 27% had focal spikes waves and 63% generalized epileptiform spikes. Comparing this study with another retrospective study done by Falope et al in Nigeria, which used similar methodology though they included children, they found epileptiform pattern among adult patients to be 39%. Among the patients with epileptiform pattern in the whole group, 92% had focal and spikes waves and 8% with generalized spikes. Studies on EEG show that abnormalities in initial EEG can be picked in up to 55% of patients and if the EEG is done serially especially within first 7 days postictal, the yield can reach 92%[56,57]. It is known that abnormal EEGs are associated with poor prognosis and worse if it is focal spikes and waves[58]. Since most of the patients with poor control had focal seizures, it is not surprising that epileptiform pattern were found in them.

Twenty seven percent patients in this study had brain CT scans. Although it was not statistically significant among the groups, most of the CT scan findings were normal (76%). Brain infarcts followed by brain atrophy were the main abnormalities found in the

CT scans. Comparing this study with another community-based study in Benghazi Libya, in which all patients with epilepsy had CT scan of the head done, they found only 9% of them have abnormal findings. The abnormal CT scan findings included 13 primary or secondary seizures tumors, 22 focal atrophies, 3 porencephalies, 4 hemorrhages, and 8 infarction.[59] Studies in Mexico showed that arachnoiditis and hydrocephalus secondary to meningeal inflammation (25.7%) were the commonest forms, whereas parenchymatous form of neurocysticercosis (NCC) is common in India[60]. In our study the number of CT scans done were few and we cannot make a lot of conclusions. It is known that most CT scans done epileptic patients are normal, but the abnormalities found depend on the prevalent neurological disease in that locality.

Seventy percent of the total group of patients was on single anticonvulsant drug. Seventy six percent of well controlled were on monotherapy as compared to 63% who were poorly controlled and was not found to be statistically significant. It is well known that with monotherapy treatment after good seizure classification one can achieve epilepsy control in 70-80% of the patients and additional 10-15% of the patients with combination therapy. Whichever drug used alone for the right type of seizures in the optimum dose can control seizures without producing unacceptable side effects and in the most appropriate formulation[61, 62].

Among the AEDs studied, Carbamazepine and phenytoin were the most frequently prescribed antiepileptic drugs as single therapy or in multiple regimens. Lisk's study done in 1984 showed that most patients were using phenytoin followed by phenobarbitone[31]. WHO recommends use of phenobarbitone as first line drug in most seizure types because of its low cost and availability in the developing countries.

Carbamazepine is the most widely used antiepileptic in the western countries. A study comparing effectiveness of carbamazepine and lamotrigine showed that there was no statistical significant difference between the two drugs in terms of efficacy though lamotrigine had fewer side effects and compliance dropouts. [55,63,64]. The newer drugs have some special indication and side effect profile advantage.

Twenty three percent of patients in this study were using alternative therapies like herbs and prayers and mainly poorly controlled patients though it was not statistically significant. A Malawian study found almost half of the patients often visit traditional healers although were not willing to admit initially[65]. Another community-based study in Nigeria, found 32.5% questioned admitted to combining medical treatment with traditional or church healing[66]. Alternative therapies are not well studied hence they might be epileptogenic or in combination with anticonvulsants might interfere with their pharmacokinetics hence leading to poor epilepsy control.

Lisk found drug noncompliance among epileptic patients to be 30% and this situation is worse 20 years later with this study finding the prevalence at 40%. In our study, the poorly controlled patients miss their medication for longer duration than well-controlled patients and this is associated with poor epilepsy control. The high rate of poor drug adherence has been shown in several studies in developing countries. Between 30% and 40% of epileptic patients appear to be noncompliant with their drug regimen (the range is 20% to 75%)[19]. In a survey of black epileptics in South Africa[20], an overall non-compliance rate of 50% was found. The reasons why patients missed their medication were due to financial difficulties, forgetfulness, and unavailability of drugs.

Serum drug levels are requested for a certain indication like in this study they were used to assess drug compliance. There is often no clear distinction between effective, ineffective, and possible toxic blood levels of AEDs. Therapeutic effects without toxicity may therefore occur outside the population range while toxicity may be seen within the same range. Sixty one percent of the random serum drug levels done were sub therapeutic as compared to a South African study among children, which showed 30% of them, did not have trace of AEDs in their serum[21]. The average random serum drug levels and 24-hour AED drug doses were higher among poorly controlled patients as compared well-controlled patients. Patients with difficult seizures to control need higher doses of anticonvulsant drug(s) thus higher average random serum drug levels and 24-hour AED drug doses among poorly controlled patients.

STUDY LIMITATIONS

1. Random serum drug levels were primarily used to assess drug adherence. Different drugs have different peak and trough levels and yet we used a single blood sample to assess random serum drug levels of different drugs.
2. Not all anti-epileptic drugs in the market were analysed due to cost and unavailability of the laboratory kits locally. These were in case very few patients.
3. Each patient had to have a single EEG done. Patients with previous EEG did not have to repeat another one; hence the EEG findings were used in the analysis. Those patients without previous EEG were sent for EEG at the time of the study.
4. Selection bias: Many patients were excluded due to incomplete data i.e. EEGs findings and some were using newer anti-epileptic drugs. Those excluded were not analysed for comparison, hence they could have different characteristics like demographic data, seizure type, or drug taking behaviour, which can affect the results of the study.

CONCLUSION

- Prevalence of poorly controlled epilepsy at KNH is 40%.
- Poor drug adherence was found to be the main contributor to poor control of epilepsy.
- Financial difficulties were the main reason contributing to poor drug adherence.
- Partial type of epilepsy was found to be associated with poor control of epilepsy.

RECOMMENDATION

1. Health education and counseling of patients especially those who forget their medications should be encouraged to improve drug compliance and epilepsy control.
2. There is need to improve accessibility of antiepileptic drugs at affordable cost.
3. A prospective study is needed with complete documentation of EEGs and other investigations including CT scan head to establish the cause and classification of seizures.

APPENDIX 1- SEIZURE STUDY

Factors associated with poor control of epileptic patients at KNH neurology clinic.

Date----------

Name----------

Case number----------

OPD number----------

Age---------- Sex M 1 F 2

Residence----------

Education level

1) No formal education 2) Primary 3) Secondary 4) Tertiary

Occupation

1) Businessperson 2) Formal employment 3) Unemployed

4) Informal sector i.e. Jua Kali, hawker. 5) Student

Seizure Characteristics

When did you have the first seizure ----------

Average seizures over the last three-month----------

What in your own opinion do you think is the cause of your illness? ----------

---

Do you have history of trauma? 1) Yes 2) No If yes when? ----------

Is there any one in your family with similar illness?

1) Yes 2) No 3) Unknown

If yes who? 1) Other siblings 2) Parents 3) Grandparents

4) Cousins 5) Uncles/ Aunts 6) others (specify)----------

Medication

What drugs are you currently on 1) Carbamazepine 2) Phenytoin 3) Phenobarbitone 4) Valproic acid 5) Others ----------

List any other medications you are taking----------

How long have you been on medication----------?

Who gives you the medication? ----------

What side effect(s) have you experienced?

1) Sedation 2) Ataxia/ In coordination 3) Bone marrow suppression i.e. anaemia 4) Skin lesions 5) Hirsutism 6) Others (specify)---------

What has been the effect of medication on your illness?

1) Improvement 2) No effect 3) Worsened

With all medications we do sometimes forget to take medicine, in your experience do you have any occasions that you forgot to take your medication?

1) Yes 2) No

If yes in the last month can you estimate for how many days you may have missed? ------

---

Are there any factors that caused you to missed medication?

1) Side effects 2) Unavailability 3) Financial difficulties

4) Stopped by a Doctor 5) Inaccessibility

6) Others (specify)----------

15. Have you used alternative medications/ therapeutic approach? 1) Yes 2) No

If yes what form? 1) Herbs 2) Prayers 3) Acupuncture 4) Others ----

What in your opinion do you expect the drugs to do?

1) Cure 2) Improve 3) No effect 4) Do not know

Investigations

Random serum drug levels

Drug	Dosage	Time of last dose	When started
Carbamazepine			
Phenytoin			
Phenobarbitone			
Na^+ Valproic			
Total			

19. EEG findings. 1) Normal 2) Generalised epileptiform spikes

3) Focal spike and waves 4) others----------

Ct scan findings----------

20. Type of epilepsy

1) Partial seizures 2) Primarily generalised seizures 3) Unclassified seizures

APPENDIX II-1

CLASSIFICATION O F E PILEPTIC SEIZURES: I NTERNATIONAL LEAGUE AGAINST EPILEPSY CLASSIFICATION (1989)

1) Partial (focal, local) seizures
    a) Simple partial seizures (consciousness not impaired)
        1) With motor signs
        2) With somatosensory or special sensory symptoms
        3) With autonomic symptoms
        4) Compound forms
    b) Complex partial seizures (with impairment of consciousness)
        1) Simple partial followed by impairment of consciousness
        2) Impairment of consciousness at onset
    c) Partial seizures with secondary generalization
2) Generalized seizures (convulsive or nonconvulsive)
        a) Tonic-Clonic (grand mal)
        b) Petit mal (absence)
        c) Atonic (drop attack)
        d) Tonic
        e) Clonic
        f) Myoclonic

3) Unclassified epileptic seizures (with incomplete data)

APPENDIX II-2

CLASSIFICATION OF EPILEPSIES AND EPILEPTIC SYNDROMES

The following is an outline of the International Classification of Epilepsies and Epileptic Syndromes. *

1. Localisation-related (focal, local, partial) epilepsies and syndromes.

Idiopathic (with age-related onset).

Benign childhood epilepsy with Centro temporal spikes.

Childhood epilepsy with occipital paroxysms

Primary reading epilepsy

Symptomatic

Chronic progressive epilepsia partialis continua of childhood (Kojewnikow's syndrome)

Syndromes characterized by seizures specific modes of precipitation (for example, reflex epilepsy)

Temporal lobe epilepsies (amygdalohippocampal, lateral)

Frontal lobe epilepsies (supplementary motor, cingulate, anterior frontopolar, orbitalfrontal, dorsolateral, opercular, motor cortex).

Parietal lobe epilepsies

Occipital lobe epilepsies

Cryptogenic

2. Generalized epilepsies and syndromes

Idiopathic (with age-related onset)

Benign neonatal familial convulsions

Benign neonatal convulsions

Benign myoclonic epilepsy in infancy

Childhood absence epilepsy (pyknolepsy)

Juvenile absence epilepsy

Juvenile myoclonic epilepsy (impulsive petit mal)

Epilepsies with grand mal seizures (generalized tonic-clonic seizures) on awakening

Other generalized idiopathic epilepsies not defined above

Epilepsies with seizures precipitated by specific mode of activation

Cryptogenic or symptomatic

West syndrome (infantile spasms, Blitz-nick-Salaam Krampfe)

Lennox-Gastaurt syndrome

Epilepsy with myoclonic-astatic seizures

Epilepsy with myoclonic absence

Symptomatic

Nonspecific cause

Early myoclonic encephalopathy

Early infantile epileptic encephalopathy with suppression-burst

Other symptomatic generalized epilepsies not defined above

Specific syndromes

Epileptic seizures complicating disease states

Epilepsies and syndromes undetermined whether focal or generalized

With both generalized and focal seizures.

Neonatal seizures

Severe myoclonic epilepsy in infancy

Epilepsies with continuous spike-wave activity during slow-wave sleep

Acquired epileptic aphasia (Lindau-Kleffner syndrome)

Other undetermined epilepsies not defined above

Without unequivocal generalized or focal features

Special syndromes

Situation-related seizures

Febrile convulsions

Isolated seizures or isolated status epilepticus

Seizures occurring only with acute metabolic or toxic event

Adopted from: Commission on Classification and Terminology of the International League Against Epilepsy. Proposal for revised classification of epilepsies and epileptic syndromes. Epilepsia 1989; 30:389-99.

APPENDIX III

Factors Leading to Noncompliance

LIMITED ACCESS TO MEDICATIONS

Driving inability or transportation difficulty

Lack of time to obtain medications

Inadequate or nonexistent reimbursement by health insurance plans (cost)

INCREASED COMPLEXITY OF DOSING REGIMEN

Inconvenience

Frequent or complicated dosing schedule

Polytherapy

Anxiety or confusion over medication regimen

Misunderstanding instructions

POOR EDUCATION

Lack of instructions on how to use medications

Lack of patient information about disease

Poor understanding of reason for medication

MEDICAL FACTORS

Medication adverse effects (impaired cognition)

Cognitive effects of seizures

Other co morbid conditions

Memory loss due to brain damage

Forgetfulness

PSYCHOSOCIAL FACTORS

Weak emotional support by family or friends

Poor relationship with health care personnel

Fear of addiction or adverse effects

Denial of disease

Financial distress

Discontinuing anti-epileptic drugs (AED) to see if they are cured

Trouble with life's responsibilities and hardships

Decreased seizure frequency causing patients to have a more lax attitude toward their medication

*Adopted from: Mary LW. Daniel M., Dipti P., Compliance in Epilepsy: A Review, htm. Vol. 26:08, Aug 2001.

APPENDIX IV

LABORATORY METHODS

Serum drug analysis

After filling the questionnaire, two millilitres of venous blood was taken from each patient and sent to Nairobi Hospital in a clean plain bottle. The sample obtained was kept until complete clot formation had taken place prior to centrifugation. The serum obtained was used for assay of Phenytoin, Carbamazepine, Valproic acid, and Phenobarbitone levels.

8.2.1 Phenobarbitone

The AxSYM Phenobarbital assay is the reagent system for the quantitative measurement of Phenobarbital in serum or plasma. The AxSYM Phenobarbital assay utilizes Fluorescence Polarization Immunoassay (FPIA) technology. Controls were done using AxSYM Phenobarbital Control.

The Procedure

Sampling Centre

Sample and all AxSYM Phenobarbital Reagents required for one test were pipetted by the sampling probe into wells of a Reaction Vessels (RV). Sample and solution 4 (line Diluent) were pipetted into one well of RV. An aliquot of predilution mixture, pre-treatment solution and solution were transferred into the curette of the RV.

The RV was immediately transferred into the processing centre. Further pipetting was done in the processing centre with the processing probe.

Processing Centre

A second aliquot of the predilution mixture was transferred to the curette along with the Phenobarbital antiserum and the Phenobarbital Fluorescein Tracer.

Phenobarbital from the sample and the Phenobarbital Fluorescein Tracer compete for binding sites on the antibody molecule.

8.2.2 Sodium Valproic acid

The FPIA optical assembly measured the intensity of polarized fluorescent light. The AxSYM Valproic Acid assay is the reagent system for the quantitative measurement of valproic acid in serum or plasma. The AxSYM Valproic Acid assay utilizes Fluorescence Polarization Immunoassay (FPIA) technology. Controls were done using AxSYM Valproic Acid Control.

The Procedure

Sampling Centre

Sample and all AxSYM Valproic Acid Reagents required for one test were pipetted by the sampling probe into wells of a Reaction Vessels (RV). Sample and solution 4 (line Diluents) were pipetted into one well of RV. An aliquot of predilution mixture, pre-treatment solution and solution were transferred into the curette of the RV.

The RV was immediately transferred into the processing centre. Further pipetting was done in the processing centre with the processing probe.

Processing Centre

A second aliquot of the predilution mixture was transferred to the curette along with the Valproic Acid antiserum and the Valproic Acid Fluorescein Tracer.
Valproic Acid from the sample and the Valproic Acid Fluorescein Tracer compete for binding sites on the antibody molecule.

8.2.3 Phenytoin

The FPIA optical assembly measured the intensity of polarized fluorescent light.

The AxSYM phenytoin assay is the reagent system for the quantitative measurement of Phenobarbital in serum or plasma. The AxSYM phenytoin a ssay utilizes Fluorescence Polarization Immunoassay (FPIA) technology. Controls were done using AxSYM Phenytoin Control.

The Procedure

Sampling Centre

Sample and all AxSYM Phenytoin Reagents required for one test were pipetted by the sampling probe into wells of a Reaction Vessels (RV). Sample and solution 4 (line Diluent) were pipetted into one well of RV. An aliquot of predilution mixture, pre-treatment solution and solution were transferred into the curette of the RV.

The RV was immediately transferred into the processing centre. Further pipetting was done in the processing centre with the processing probe.

Processing Centre

A second aliquot of the predilution mixture was transferred to the curette along with the Phenytoin antiserum and the Phenytoin Fluorescein Tracer. Phenytoin from the sample and the Phenytoin Fluorescein Tracer compete for binding sites on the antibody molecule.

8.2.4 Carbamazepine

The FPIA optical assembly measured the intensity of polarized fluorescent light. The AxSYM Carbamazepine assay is the reagent system for the quantitative measurement of Phenobarbital in serum or plasma. The AxSYM Carbamazepine assay utilizes Fluorescence Polarization Immunoassay (FPIA) technology. Controls were done using AxSYM Carbamazepine Control.

The Procedure

Sampling Centre

Sample and all AxSYM Carbamazepine Reagents required for one test were pipetted by the sampling probe into wells of a Reaction Vessels (RV).

Sample and solution 4 (line Diluent) are pipetted into one well of RV.

An aliquot of predilution mixture, pre-treatment solution and solution were transferred into the curette of the RV.

The RV was immediately transferred into the processing centre. Further pipetting was done in the processing centre with the processing probe.

Processing Centre

A second aliquot of the predilution mixture was transferred to the curette along with the Carbamazepine antiserum and the Carbamazepine Fluorescein Tracer.

Carbamazepine from the sample and the Carbamazepine Fluorescein Tracer compete for binding sites on the antibody molecule.

The FPIA optical assembly measured the intensity of polarized fluorescent light.

APPENIX V

CONSENT EXPLANATION

I am Dr. Mativo from the University of Nairobi and am doing a study on the management of epilepsy. I recruited you randomly to participate in my study. Can I talk to you in private?

I kindly wish to inform you that the study is part of fulfilment of my postgraduate programme. The study will involve epileptic patients who are well controlled i.e. without frequent fits and those poorly controlled. The aim of the study is to see why some epileptic patients are controlled and others not. The study will include filling a questionnaire, checking your medical records and taking a random blood sample for drug analyses. The information to collect includes participant demographic data, drug taking behaviour, and seizure characteristics. I will scrutinize your file for documentation of EEG and CT scan findings as well as serum anti-epileptic drug analysis to check if the drug levels are adequate. I will personally do all the above as the principal investigator.

Participation in the study is a matter of your choice and it is your right to choose. Whether you choose to participate or not will not affect your medical care. The results will be used for managing you better since I will inform your doctor about them. They will also be extrapolated for managing other epileptic patients. At the end of the study, I will hand the study findings to the medical department in University of Nairobi.

Before I involve you in my study, I kindly request you to sign the consent form below.

Note: In-case of patients less than 18 years, the explanation will be done to the guardian/parent. They will also be required to sign the consent form on behalf of the patient.

APPENDIX VI

CONSENT FORM

I, (patient)_____I hereby give consent to participate in this study. I have been fully informed about the research conduct. All the data shall be handled confidentially and the identity of participants shall be concealed. I am at liberty to withdraw from the study and this will not affect the normal care.

Signature

APPENDIX VII

CONSENT FORM

I, (parent /guardian)_____of _____I hereby give consent my child/relative to participate in this study. I have been fully informed about the research conduct. All the data shall be handled confidentially and the identity of participants shall be concealed. I am at liberty to withdraw from the study and this will not affect the normal care.

Signature

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