CLINICAL AUDIT OF ACUTE SEIZURE MANAGEMENT IN PAEDIATRIC PATIENTS AT KENYATTA NATIONAL HOSPITAL

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DEPARTMENT OF PHARMACOLOGY, CLINICAL PHARMACY AND PHARMACY PRACTICE

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LIST OF ABBREVIATIONS

AC: Actual Criterion

AED: Antiepileptic drug

AIDS: Acquired immunodeficiency syndrome

ASS: Acute symptomatic seizure

CME: Continuous Medical Education

CNS: Central Nervous System

CSE: Compulsive status epilepticus

CSF: Cerebral Spinal Fluid

CT: Computerized tomography

FS: Febrile seizures

HIV: Human Immunodeficiency Virus

ILAE: International League against Epilepsy

KNH: Kenyatta National Hospital

MC: Maximum Criterion

NHS: National Health Services

MRI: Magnetic Resonance Imaging

NICE: National Institute for Health and Care Excellence

SJS: Stevens-Johnson syndrome

TEN: Toxic epidermal necrolysis

UoN: University of Nairobi

OPERATIONAL DEFINITIONS

Acute seizures are seizures related to febrile illness or acute neurological insult and include febrile seizures and acute symptomatic seizures.

Acute symptomatic seizures are seizures associated with acute neurological insult caused by metabolic abnormalities, toxins, structural deficits, neurological infections (such as complicated malaria, bacterial meningitis or encephalitis) or inflammation.

Antiepileptic drugs are drugs used to control seizures.

Clinical audit is a quality improvement process that seeks to improve patient care and outcomes through a systematic review of care against explicit criteria and implementation of change.

Epilepsy is a neurological disorder characterized by recurrent seizures and is defined by two or more unprovoked seizures.

Febrile seizures are defined as seizures associated with fever (≥38.5°C) in absence of neurological involvement in children aged 1 month – 6 years.

Performance threshold/level of performance/standard is a defined level or degree of expected compliance normally expressed as a percentage.

Quality of care is the level at which delivery of health services leads to desired health outcomes as per current clinical practice guidelines.

Seizures are the transient occurrence of signs and symptoms due to abnormal excessive or synchronous neuronal activity in the brain.

Treatment gap is the difference between the number of people with active epilepsy or seizure disorder and the number of those whose seizures are appropriately treated in a given population at a given time.

ABSTRACT

Background

In children, acute seizures are associated with a heightened risk of future development of epilepsy. Therefore, effective control of acute seizures is crucial in the reduction of the burden of epilepsy. Antiepileptic drugs offer seizure control in a variety of seizure disorders, epilepsy and epilepsy syndromes. Challenges in managing those with epilepsy and seizures include inappropriate use of antiepileptics due to non-adherence to treatment guidelines, intolerance to adverse effects, and lack of adequately stocked hospitals. Inadequate management of seizures can lead to poor outcomes related to cognitive and behavioural disabilities and in worst cases, death. It is therefore important to evaluate the practice of seizure management. However, presently there are no local studies outlining the current practice in seizure management or assessing the processes and outcomes of seizure management in Kenya.

Objectives

To conduct a clinical audit of acute seizures in paediatric patients admitted at Kenyatta National Hospital.

Methods

A descriptive cross-sectional study was done to find out the characteristics, management and outcomes of acute seizures among paediatric in-patients at Kenyatta National Hospital (KNH). In-patient medical records of 97 children admitted with acute seizure during the study period of December 2019 to January 2021 were sampled by consecutive sampling and data extracted. A Clinical Audit tool was developed and used to assess the structures, processes and outcomes of acute seizure management of paediatric in-patients at Kenyatta National Hospital. The results obtained for each criterion was compared to pre-set standards for each criterion.

Results

The patients' records sampled consisted of 97 children with 54 of them being male and 43 being female aged between 1 month and five years who were admitted at the hospital for acute seizure management. Analysis of patient records showed that most patients had febrile seizures 56 (58%) than acute symptomatic seizures 41 (42%) that were generalized tonic clonic in nature. Bacterial meningitis was the most common 39 (41%) cause of acute seizures. The most

common AED used for initiation and maintenance dosing either as monotherapy or combination therapy was Phenobarbital. This coincides with data showing the most frequent acute seizure type to be generalized seizures as Phenobarbital is one of the recommended AEDs for seizure control. Also, most patients 70 (72%) had their seizures controlled after hospitalisation. There was poor recording of adverse drug reactions due to antiepileptic drugs and none of the patient files had this information.

The clinical audit revealed that there were gaps in the safe and effective use of antiepileptic drugs during acute seizure management in paediatric patients at Kenyatta National Hospital and recommendations made to improve on areas of non-compliance.

Conclusion

An evidence-based tool was developed for audit of acute seizure management. This was successfully used to audit structures, processes and outcomes that characterize acute seizure management. Some criteria had full compliance to the pre-set standards such as proper assessment, classification and laboratory investigations in acute seizure management as well as having adequate staff. Areas of partial and non-compliance to set standards included lack of a few critical essential antiepileptic drugs and safe and effective use of antiepileptic drugs respectively. A quality improvement plan was developed for use by the Kenyatta National Hospital management.

CHAPTER ONE: INTRODUCTION

1.1 Background

Epilepsy and seizures are common and one of the oldest conditions known to mankind. Seizures are a result of excessive electric impulses discharge of cerebral neurones (1) and are characterized by physical manifestations like lip-smacking, tongue biting, falling, incontinence and rhythmic jerks. Furthermore, there may be presence or absence of consciousness depending on the seizure type (2). Epilepsy is a neurological disorder characterized by recurrent seizures and is defined by two or more unprovoked seizures (3). Diagnosis of epilepsy is only restricted to those with recurring seizures, at least twice in a year (4).

At least 5% of the world population have a likelihood of experiencing a single seizure in their lifetime (5). However, the prevalence and incidence of specific seizure types and epilepsy syndromes are not well documented (3).Globally, the incidence of epilepsy and seizure disorders has been estimated as 50-60 per 100,000 persons years (6). In developing countries such as Kenya, epilepsy is more common as compared to developed countries. This is as a result of increased risk of having conditions that lead to brain damage such as malaria, trauma, meningitis, pre and perinatal complications and HIV/AIDS (3). In a systematic review done based on current Kenyan literature, it was found that, in children, the prevalence of lifetime epilepsy was 21-41 per 1000 and the incidence of active convulsive epilepsy was 39-187 cases per 100 000 per year. Among Kenyan children, active convulsive epilepsy is common with only 7-29% on antiepileptic medication (7).

A large proportion of childhood epilepsy remains untreated leading to poor outcomes such as physical injuries, psychiatric and neuropsychosocial impairment, social disability, short lifespan and death (8). Uncontrolled epilepsy negatively impacts their education, quality of life and psychosocial development. Therefore, it is beneficial to effectively control seizures in patients with epilepsy and seizure disorders in order to improve their quality of life (8,9). A study done in Kilifi found that 28/900 (3.1%) of children died following acute seizure episodes and had Meningitis, Malaria and viral encephalitis. After hospital discharge, 11/900 (1.3%) of children had gross neurological deficits with disabilities such as hearing loss, motor deficits and speech impairment (10). This was due to barriers to treatment such as underdiagnosis, limited access to appropriate health facilities and medications. Also, cultural practices and

beliefs cause social exclusion due to stigmatization hence affecting seeking of medical services (7).

Seizure management by use of antiepileptic drugs is imperative in providing seizure control in epilepsy and seizure disorders. There are several classes of antiepileptic drugs and various regimens used in the management of different seizure subtypes and epilepsy syndromes. The goal of management of seizures by use of antiepileptics is control of seizures with the occurrence of minimal side effects. Despite the beneficial effects that antiepileptic drugs (AEDs) give in seizure management, it is mandatory to note that they are high alert medicines that can harm the patient when used in error (11). Unfortunately, untoward outcomes may arise from the use of antiepileptics. For instance, behavioural and cognitive adverse effects have been observed in children on AEDs (for example, phenytoin, phenobarbital, and carbamazepine) such as deterioration of memory, language and learning capabilities. Depression, psychosis, restlessness and hyperactivity are also reported. This is mainly observed when higher doses than required are used and polytherapy of AEDs that interact to heighten adverse cognitive and behavioural side effects (12,13).

In the management of seizures and epilepsy, it is critical that the appropriate antiepileptic drug/regimen is used, tailored to a patient's type of seizure or epilepsy syndrome. Therefore, adherence to treatment guidelines by healthcare workers is vital in ensuring optimal health outcomes and reduced harm to the patient. Consequently, there is need for health facilities to conduct regular clinical audits of seizure management. A clinical audit is a quality improvement process that seeks to improve patient care and outcomes through a systematic review of care against explicit criteria and implementation of change (14). The clinical audit aims to point out any variation between actual practice and standard practice so as to identify the changes needed to improve quality of care. Clinical audits allow for routine assessment and monitoring in the healthcare institutions.

1.2 Problem Statement

AEDs are mainly indicated for management of seizures. According to the World Epilepsy Atlas, the treatment gap for management of seizures in developing countries is high, Kenya's estimated at 80% (3). A treatment gap is the difference between the number of people with active epilepsy or seizure disorder and the number of those whose seizures are appropriately treated in a given population at a given time. The main reasons for the large treatment gap are noted to be: lack of available, accessible and affordable healthcare as well as lack of awareness

(3,15). Accordingly, AEDs are included in the Kenya Essential Medicines list to ensure availability at all levels of care.

However, AEDs need proper administration, monitoring and adherence for proper seizure control. Due to their narrow therapeutic index, lack of proper use leads to medication errors that harm the patient. Also, AEDs such as phenobarbital have been shown to have adverse neurocognitive effects in children thus affecting their memory, concentration and learning abilities (16). If the wrong AED is used for a particular seizure type, mortality and morbidity is often observed (11,12). In addition, majority of AEDs have drug-drug interactions when they are co-administered with other drugs that lead to drug toxicity and treatment failure (7–9).

Guidelines and protocols are therefore available to assist healthcare providers in optimizing care with minimal harm to the patient. In Kenya, the following guidelines offer direction as regards to seizure management: Kenya National Guideline for Management of Epilepsy: A practice guide for healthcare workers (2016), Clinical guidelines for Diagnosis and Treatment of Common Conditions in Kenya (October 2002), Clinical Guidelines for Management and Referral of Common Conditions at Level 4-6: Hospitals (2009), Basic Paediatric Protocols (2016) and the KNH Formulary for use at the Kenyatta National hospital. Adherence to these clinical guidelines needs to be regularly assessed in order to ensure that patients are receiving optimal care. However, such monitoring is not routinely done.

1.3 Study Justification

Acute seizures are common in paediatric patients due to various aetiologies such as infections, and management using AEDs should be according to set standards and protocols. This is due to the narrow therapeutic nature of AEDs and drug interactions that lead to drug toxicity. Also, poor management of acute seizures leads to poor prognosis and neurological, emotional and behavioural adverse outcomes in the affected child as well as development of epilepsy (17–19).

Adherence to clinical guidelines for management of seizures ensures optimal health outcomes are achieved with minimal adverse effects. Treatment failure in those with epilepsy and seizures is largely attributed to intolerance to adverse effects and inadequate seizure control due to inappropriate use of antiepileptics. Lack of adequately stocked hospitals and limited accessibility to hospitals may further contribute to the inadequate management of a large number of seizure patients.

In order to better understand and address this problem in Kenya, it is important to evaluate the practice of seizure management. However, presently there are no local studies outlining the current practice in seizure management or assessing the processes and outcomes of seizure management in Kenya despite the large treatment gap. This study sought to fill this gap in knowledge through the conduct of a clinical audit at a national referral hospital by establishing whether the National guidelines are adhered to in the management of seizures in in-patient paediatric patients, and how current practice compares to well-defined and established standards.

The findings of the clinical audit will be used to inform changes to enhance quality of care as well as safety to the paediatric patients with seizures at KNH by ensuring that acute seizures are properly managed and treatment outcomes achieved. Acute seizures that are poorly managed become refractory to treatment, leading to future development of epilepsy and other negative outcomes such as neurological impairment, behavioural and emotional dysfunctions. The hospital will also benefit from this clinical audit as the areas of non-compliance have been highlighted and recommendations given on how to make improvements The audit tool that has been developed during the course of this audit will be available to allow for re-evaluation of seizure management after a specified timeframe to check if any improvements have been made.

Other health institutions could benefit from adopting the clinical audit tool developed in this study for their own clinical audits when evaluating seizure management in their institutions as well as compare findings of the study to their own findings.

1.4 Research Questions

1. What are the types and causes of acute seizures in paediatric patients admitted at KNH?
2. How are acute seizure episodes in paediatric patients admitted at KNH managed?
3. How do the structures, processes and outcomes associated with management of acute seizures in paediatric patients at KNH compare to evidence-based audit criteria?

1.5 Objectives

1.5.1 Main Objective

To conduct a clinical audit of acute seizures in paediatric patients admitted at Kenyatta National Hospital.

1.5.2 Specific Objectives

1. To determine the types and aetiology of acute seizure episodes in paediatric patients admitted at KNH.
2. To describe the pharmacological management of acute seizure episodes in paediatric patients admitted at KNH.
3. To audit the structures, processes and outcomes of current in-patient management of acute seizure episodes in paediatric patients admitted at KNH.

CHAPTER TWO: LITERATURE REVIEW

2.1 Definition and Classification of Seizures

According to the International League against Epilepsy (ILAE), a seizure is a transient occurrence of signs and symptoms due to abnormal excessive or synchronous neuronal activity in the brain (20). In the pathophysiology of seizures, there is synchronous abnormal discharge of a network of neurones which arise from excess excitation or loss of inhibition. The abnormal discharges can be localized or spread to other areas of the brain affecting more neurons. The neural networks originate from the cortical, subcortical, limbic region and brainstem. The region of the brain where a seizure originates is known as epileptic foci (2,21).

Seizures are classified according to clinical presentation or underlying pathology. The three major seizure types are focal seizures, generalized seizures and seizures of unknown onset. Focal seizures are characterized by seizures that are localized in one hemisphere of the brain while generalized seizures involve simultaneous abnormal neuronal discharges in both hemispheres of the brain. If a seizure cannot be classified as either focal or generalized, it is categorized as seizure of unknown onset. According to the revised ILAE 2017 classification of seizures, the term ‘partial’ is referred to as focal and the terms ‘simple’ and ‘complex’ replaced with awareness and impaired awareness respectively (22).

2.1.1 Focal seizures

In focal seizures, clinical manifestations depend on the cortical area activated. Focal seizures are mainly divided according to presence or absence of consciousness. In presence of consciousness, it is termed as focal aware seizures. In absence of consciousness, it is termed as focal with impaired awareness. Following this, subdivision is done based on motor or non-motor (absence) characteristics. Motor onset is characterized by automatisms (for example, lip smacking, chewing, fumbling), tonic, clonic, myoclonic, atonic, hyperkinetic or epileptic spasms. Non-motor onset includes behavioural arrest, autonomic (for example, tachycardia, pallor), cognitive, sensory and emotional seizures (2,3).

Manifestations of Focal aware seizures are diverse and dependant on the area of the cortex activated by the seizure. It lasts 20-60 seconds. In Focal with impaired Awareness, there are aimless movements such as smacking of lips and impaired consciousness lasts 30 seconds to 2 minutes. If the focal seizure progresses into a tonic-clonic seizure with bilateral involvement it

is referred to as focal to bilateral tonic-clonic seizure (previously known as secondary generalized seizures) and typically lasts 1-2 minutes (2,3).

2.1.2 Generalized seizures

Generalized seizures are primarily divided into motor and non-motor (absence) seizure types. Motor seizures may be tonic, clonic, myoclonic, atonic or tonic-clonic. In tonic seizures, there is sudden stiffening of extensor muscles causing falls if one is standing. Tongue biting and clenching of teeth may occur. Clonic seizures are associated with rhythmic jerks. Myoclonic seizures are characterized by brief muscle contraction which may be restricted to an extremity or generalized (21). Atonic seizures are associated with abrupt loss of muscle tone involving head, trunk or limbs causing the patient to fall. This is mostly observed in patients with early onset of severe epilepsy from infancy (2).

In generalized tonic-clonic seizures, the tonic phase is characterized by spasms of all muscles for a short period; breathing is affected causing cyanosis. The clonic phase is characterized by rhythmic contraction and relaxation of muscles for a longer period causing jerks. Incontinence and tongue biting may occur. On recovery, the patient experiences confusion, drowsiness, headache and sleepiness (2).

Absence seizures are classified as typical or atypical depending on level of consciousness. In typical absence seizures, there is impaired consciousness characterized by blank stares with or without lip-smacking. Normally, it lasts 5-10 seconds and can be confused with day dreaming (3). It is common in children between 5-15 years and may be accompanied by clonic movements of eyelid and eyebrows (eyelid myoclonia), mouth and face (myoclonic absence) (2). Atypical absence seizures have minimal impairment of consciousness and less abrupt. They are characterized by gradual loss of muscle tone of trunk and limbs and faint muscle jerks. The patient may perform tasks slowly or with mistakes.

2.1.3 Seizures of unknown onset

Seizures of unknown onset (unclassified seizures) are difficult to categorize as either focal or generalized. For instance, epileptic spasms which are associated with sudden extension, flexion or both of the head, neck, trunk and upper extremities lasting 1-2 seconds (2,3).

Table 1 below summarizes classification of seizures types and outlines the different seizure subtypes (22).

Table 1: Classification of seizures

FOCAL ONSET
Aware/Impaired awareness
Motor onset: automatisms, atonic, clonic, epileptic spasms, hyperkinetic, myoclonic, tonic
Non-motor onset: autonomic, behaviour arrest, cognitive, emotional, sensory
GENERALIZED ONSET
Motor: tonic-clonic, clonic, myoclonic, atonic, epileptic spasms
Non-motor(absence): typical, atypical, myoclonic, eyelid myoclonia
UNKNOWN ONSET
Motor: tonic-clonic, epileptic spasms
Non-motor: behaviour arrest

Besides the classification of seizure types, there is classification of epilepsy syndromes into three main classes: Generalized, Focal and Undetermined (20,22). There are more than 50 epilepsy syndromes identified. Classification is based on clustering of symptoms occurring simultaneously, seizure type, age of onset of seizure type, aetiology and other factors (3,21).

2.2 Acute seizures

2.2.1 Prevalence and Incidence of Acute seizures

Acute seizures are seizures related to febrile illness or acute neurological insult, and include febrile seizures and acute symptomatic seizures (19,23). Febrile seizures are defined as seizures associated with fever (≥38.5°C) in absence of neurological involvement in children aged 1 month – 6 years (17,24). Acute symptomatic seizures are defined as seizures associated with acute neurological insult caused by metabolic abnormalities, toxins, structural deficits, neurological infections (such as complicated malaria, bacterial meningitis or encephalitis) or inflammation (17,23,25). Prognosis of acute symptomatic seizures is poorer than febrile seizures. Due to difficulties distinguishing between febrile seizures and acute symptomatic seizures in Africa, acute seizures is the term used to describe seizures with fever in Sub-Saharan Africa (19).

In European and American studies, the prevalence of febrile seizures is 2-5 % (26). Unfortunately, there are minimal epidemiological studies on acute seizures with most estimates from hospital studies, thus underestimating the burden. In a study done in Kenya, the

prevalence of acute seizures was found to be 6.1% translating to 2.9% for febrile seizures and 3.2% for acute symptomatic seizures (19). Other studies done in Kilifi, Kenya found the incidence of acute seizures in children aged 0-13 years admitted in hospital to be 425-650/100,000/year though this might be an underestimation of the true incidence as many children are not admitted after an episode of acute seizure (19,27). In Tanzania, the prevalence of febrile seizures was found to be 2.1% and was mostly attributed to *falciparum* malaria (28).

2.2.2 Types of Acute seizures

Acute seizures are classified based on their observable characteristics as either single/repetitive, focal/generalized, simple/complex or short/prolonged. The prognosis of acute seizures depends on the severity of the acute seizure type and aetiology. Table 2 shows detailed definitions of the types of acute seizures based on ILAE recommendations (4,20,25).

Table 2: Types of Acute seizures

Types of Acute seizures	Definition
Single	A single seizure episode in current illness
Repetitive	More than one seizure episode in the current illness
Focal	Seizures involving one body part
Generalized	Seizures involving entire body parts
Simple	Seizures that are incidental and are tonic-clonic excluding complex seizures.
Complex	Seizures that are focal, repetitive, prolonged (including status epilepticus).
Short	Seizures that last ≤ 10 minutes.
Prolonged	Seizures that last ≥10 minutes
Convulsive Status epilepticus	Seizures lasting ≥ 30 minutes with loss of consciousness or intermitted seizures over a period of ≥30 minutes without regaining consciousness in between the seizures.

Convulsive status epilepticus (CSE) is a phenotype of acute seizures and is a common childhood neurological emergency that is associated with significant mortality and morbidity. The most common cause of CSE are prolonged febrile seizures, acute symptomatic events such

as meningitis and remote symptomatic event, for example, epilepsy (29). Acute bacterial meningitis has the worst outcome in terms of mortality and morbidity in children with CSE.

In a five-year Cohort study conducted in Kilifi, Kenya, the incidence of childhood CSE was found to be 23/100,000/year which is higher than that reported in developed countries, for example, London (18-20/100,000/year) (30). A high incidence of mortality from childhood CSE is recorded in Kenya due to restricted access to emergency AEDs (particularly parenteral phenobarbital), long distances to access of adequate medical treatment in hospitals, hence long-lasting seizures that are refractory to treatment. To reduce mortality, interventions should be made to prevent major causes of CSE such as malaria and bacterial meningitis (30) and prompt effective emergency seizure treatment by use of appropriate protocols such as Basic Paediatric protocols and guidelines such as the Kenya National guideline for the management of epilepsy (2,3). A proportion of Kenyan children with complex seizures associated with malaria (26%) were found to have neurological impairment 3-9 years later (27).

2.2.3 Aetiology of Acute seizures

2.2.3.1 Risk factors and causes of febrile seizures

The risk factors of developing febrile seizures include family history of febrile seizures in up to 40 % of those affected (31), developmental delays, prolonged admission in neonatal care and attendance at day-care (26).

Certain vaccines have been linked to increased risk of febrile seizures such as Diphtheria/tetanus/pertussis/hepatitis B/*H. influenza* type B vaccine (Pentavalent vaccine) (32) that is given to 6, 10 and 14-week old infants in Kenya (33), H1N1 influenza vaccine (34), and measles-containing vaccines such as Mumps/Measles/Rubella (MMR) vaccine (35) given to infants in Kenya at 9 and 18 months (33). The duration and extent of fever have also been shown to increase the risk of febrile seizures (36).

Worldwide, the main causes of febrile seizures are viral infections such as human herpes viruses (HHV) 6 and 7 (37,38), respiratory syncytial virus, influenza A, adenovirus, and parainfluenza. In Oriental countries such as Hong Kong, China and Japan, these viruses attribute to about 50% of cases of febrile seizures (38).

Other infections include otitis media, pharyngitis and *Shigella* gastroenteritis which was the main case of febrile seizures in Turkish children (39). In tropical sub-Sahara Africa including

Kenya, *falciparum* malaria is the most common cause of febrile seizures as it induces fever (40).

Iron deficiency has been linked to febrile seizures as iron is required for enzymes required for neurotransmitter synthesis such as monoamine oxidase and aldehyde oxidase (41–43). Also, other deficiencies in folic acid, vitamin B12, calcium selenium, and magnesium are associated with development of febrile seizures (36).

2.2.3.2 Risk factors and causes of acute symptomatic seizures

In the USA, the commonest causes of acute symptomatic seizures (ASS) are CNS infections such as encephalitis and meningitis, traumatic brain injury and spontaneous intracranial haemorrhage in children (44–46); In adults, alcohol withdrawal and head injury were common causes of ASS (47). In Taiwan, a study showed that the main causes of ASS are intracranial infections (such as encephalitis and meningitis), gastroenteritis and intracranial haemorrhage (48).

In tropical sub-Sahara Africa inclusive of Kenya, the commonest cause of ASS is falciparum malaria. This is closely followed by respiratory infection, acute bacterial meningitis, metabolic abnormalities (mostly hyponatremia, hypocalcaemia and hypomagnesemia (49)) and bacterial sepsis (26,27,27,50). Other minor causes of ASS in Kenya are sickle cell anaemia and hypoxic-ischaemic encephalopathy (27).

In a Cohort study done in South Africa, ASS was reported in 7.6% of children with HIV infection. This was due to the high frequency of acute bacterial meningitis, tuberculous meningitis and HIV-associated encephalitis (51). A cohort study done in HIV positive adults in Zimbabwe, found that there was a high frequency of ASS linked to high mortality and morbidity. This was attributed to opportunistic infections, metabolic abnormalities, tumours and adverse effects of Antiretroviral drugs and HIV itself (52).

2.2.4 Outcome of Acute seizures

The acute seizure type determines the risk of future epilepsy. A Kenyan study showed that there was a higher risk of convulsive epilepsy after occurrence of acute seizures 1-7 years after admission. It was found that prevalence of epilepsy was higher in acute symptomatic seizures and in convulsive status epilepticus (53). Other risk factors in conjunction with acute seizures that increased risk of developing of epilepsy were cerebral palsy and perinatal complications (17). In European and American studies, epilepsy after febrile seizure is reported in 2-8% of the children with general epilepsy being more common than focal epilepsy. In Africa, Kenya included, ASS has a greater risk than febrile seizure in development of epilepsy which can be linked to damage by intracranial infections such as malaria (17,18). Other risk factors for development of epilepsy include family history of epilepsy, shorter duration (< 1 hour) of fever before seizure, onset of FS before age of 1 year or after 3 years, repetitive FS episodes and neurodevelopmental abnormalities (36).

Prognosis of FS is favourable and is usually self-limiting and benign. However, recurrence occurs in less than 10% of the affected children. Risk factors for recurrence include short interval between onset (<1 hour) of fever and initial seizure, family history of FS and epilepsy, attendance at day care, repetitive FS in same febrile illness, if age of onset is < 15 months, first FS is complex, cold season when first seizure was experienced and if there are any neurodevelopmental delays (26,36,38).Complex febrile seizures which can be repetitive, focal or prolonged are associated with poor outcomes such as epilepsy, neuro-disability and prolonged seizure attacks.

ASS has been shown to cause poorer neurocognitive outcomes, for example, mental retardation and learning disorders compared to FS. In children with family history of mental health problems, behavioural and emotional problems such as concentration difficulties are likely to occur (26). In Kenya, emotional and behavioural problems were observed in children who had CSE 7 years later (53). Also, complex seizures attributable to severe *falciparum* malaria were associated with a higher risk of neurocognitive impairment (54).

2.3 Management of Acute seizures

Treatment of acute seizures is symptomatic and etiologic. Symptomatic seizure management is dependent on the type of acute seizure and the AEDs of choice are outlined in the basic paediatric protocols, the antiepileptic drug protocol in the Kenya National guideline for

Management of Epilepsy, the KNH formulary and summarized in Appendix E. Other comorbidities should be managed after appropriate laboratory investigations have been carried out.

2.3.1 Pharmacotherapy

AEDs are diverse pharmacological agents with various mechanisms of action that are used to manage different seizure disorders and epilepsy syndromes. They can be classified based on how long the drug has been used following approval. Since newer AEDs (approved after 1990) have not shown any superiority to classical AEDs in terms of efficacy, most are used as adjunctive treatments to standard therapy with classical AEDs (55,56). However, some newer AEDs have better tolerability, pharmacokinetics and reduced drug interactions (57). Table 3 below outlines the classification of AEDs (21,55).

Table 3: Classification of antiepileptic drugs

Classical Antiepileptic drugs	**Examples**
Hydantoins	Phenytoin
Antiseizure barbiturates	Phenobarbital, primidone
Iminostilbenes	Carbamazepine
Succimides	Ethosuximide
Benzodiazepines	Clonazepam, diazepam, lorazepam
Aliphatic carboxylic acid	Valproate
Newer Antiepileptic drugs	
Gabapentin, Pregabalin, Lamotrigine, Topiramate, Vigabatrin, Felbamate, Zonisamide	

Generally, the type of AED used for seizure management depends on the nature of the seizure. Current therapy is symptomatic, that is, current AEDs inhibit seizures; neither effective cure nor prophylaxis is available (7). In Kenya, diagnosis of seizures is mainly clinical; based on history and observation. Thus, errors in diagnosing seizures lead to use of wrong AEDs causing poor seizure control followed by increasing of drug doses and drug toxicity (58). To note, drugs used for focal seizures are the same for all subtypes of focal seizures while drugs used for generalized seizures are dependent on the subtype of generalized seizure (59).

When developing a drug therapy, single drug use is preferred for patients who are not affected severely and can gain from fewer adverse effects of monotherapy. For patients with hard to control seizures, multiple drugs are used at the same time. According to the Kenyan guideline for management of Epilepsy, 2016, when initiating treatment, one drug should be used at the lowest recommended dose. Gradually, the dose should be adjusted until complete seizure control or maximum therapeutic dose is attained. In case of lack of seizure control, a second drug should be added while reducing or maintaining the dose of the initial drug depending on the clinical response. Monitoring of plasma drug concentrations enables optimization of AEDs during initiation of therapy, after dose adjustments, due to therapeutic failure, when drug toxicity occurs or when multi-drug therapy is started. Despite monitoring plasma drug concentrations, some AEDs clinical effects do not relate with their plasma concentrations in plasma, for example., phenobarbital and benzodiazepines. The recommended dosages are just guidelines for therapy. Of importance, therapeutic regimen should be based on clinical effects and drug toxicity. According to the Kenyan guideline for management of epilepsy, drug monitoring should be done in hard-to-control seizures or where there are significant adverse effects.

When giving a combination of AEDs, awareness of treatment outcomes, pharmacokinetic properties, therapeutic levels, the side effects and potential drug interaction profile of each drug is crucial as highlighted in Appendix E.

2.4 Quality of Care

2.4.1 Clinical Audit

The standard definition of a clinical audit is a quality improvement process that seeks to improve patient care and outcomes through systematic review of care against explicit criteria and implementation of change (60). It entails reviewing clinical performance against set standards and improvement of practice followed by re-audits to drive up standards. Hence, it improves quality of care delivered, outcomes of care as well as access and timeliness of service delivery and boosts the reputation of the health facility. Globally, healthcare organizations develop and use various quality indicators for measurement of process and outcome criteria in order to measure, monitor and improve quality of care offered by healthcare institutions.

This clinical audit will establish whether current practice meets the standards of care and practice in the area of acute seizure management in paediatric patients as set out in guidelines,

in this case the Kenya National Management of epilepsy guideline, the Basic paediatric protocols and the KNH formulary.

The Donabedian model is a conceptual framework that examines health services and evaluates quality of health care. This model therefore conveniently provides a framework for the conduct of clinical audits. It is divided into three criteria: Structure, Process and Outcomes. This facilitates in coming up with the performance/quality indicators, the criteria and standards for the audit tool. A criterion is an explicit statement that clearly defines what is being measured and represents important aspects of quality of care that can be measured objectively. The audit criteria are based on updated evidence based on local and international guidelines, protocols and procedures. In this audit, selected audit criteria are derived from evidence-based data from the Kenya National Management of epilepsy guideline, the basic paediatric protocols, the KNH formulary, the NICE guidance 27 for Epilepsy in children and young people (61) and the guidelines from the American Epilepsy society (62).

In each of the three areas of evaluation, there are different criteria examined. Furthermore, each criterion has one or more indicators to be measured. Also, each indicator has a predetermined performance threshold/standard against which the measured output for the indicator is compared. The structure criteria include what is needed for provision of care. It refers to resources required for delivery of care services. These include competent and adequate staff, provision of equipment, physical space, organizational structure of the institution etc. Process criteria entail what is done for delivery of care. It comprises of actions done by healthcare workers as well as patients. For instance, assessments, prescription, dispensing, monitoring and communications. Process criteria aids in determination of the extent non-compliance and poor design influences the quality of care delivered. Outcome criteria relates to the expectation of what should happen as a result of treatment. It consists of the anticipated outcome of care. It can be patient specific such as patient satisfaction or knowledge status. Also, it can be based on clinical outcome such as physical/behavioural response and health status after an intervention. This stage is deemed as the most suitable in measurement of effectiveness of delivery of quality care services (60,63).

Figure 1 shows the structure, processes and outcome of the acute seizure management.

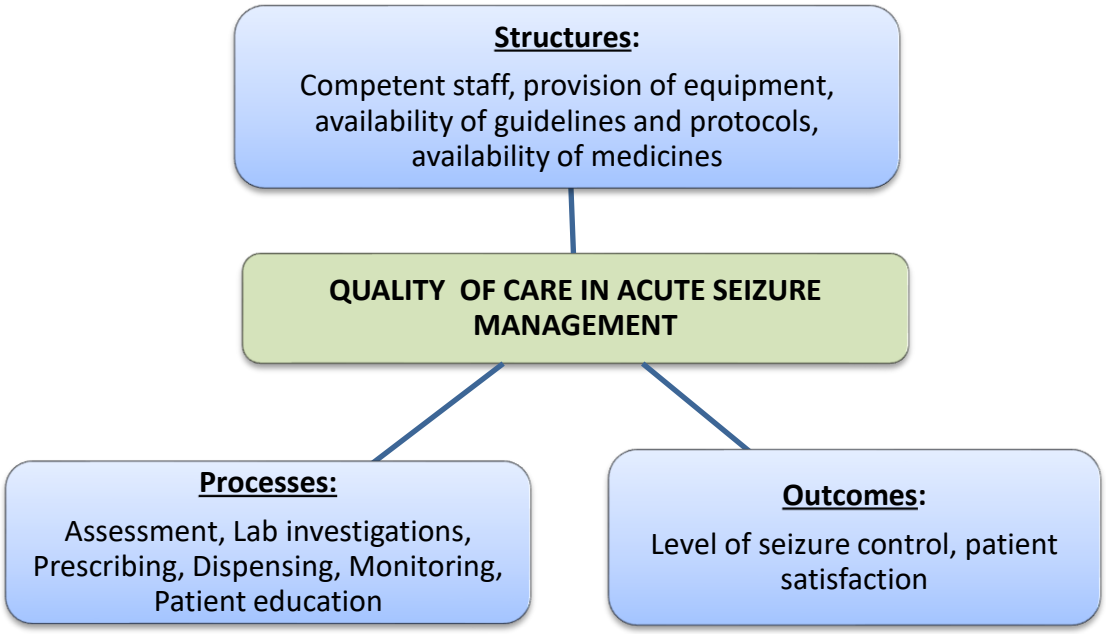


Figure 1: Quality indicators of acute seizure management (Donabedian model)

A good quality clinical audit has four main stages of activity as shown in the audit cycle in Figure 2.

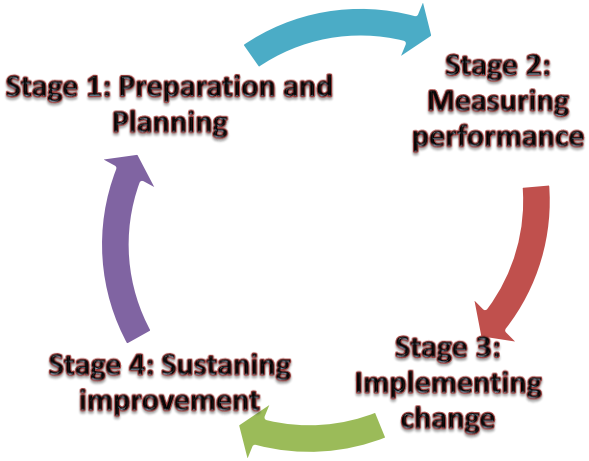


Figure 2: the Audit cycle (NICE, 2002)

Stage 1 involves preparation and planning. The first step entails choosing an audit topic that has major clinical importance, has ease of collection of data and analysis of data as well as having significant consequences. Following selection of the audit topic is selection of audit criteria and standards. Review of available evidence is carried out against which an audit is to

be done. Local and international guidelines, procedures and protocols are used to inform audit criteria. In this audit, criteria has been developed from evidence-based data from the Kenya National Management of Epilepsy guideline, the basic paediatric protocols, the KNH formulary, the NICE guidance 27 for Epilepsy in children and young people (2013) (61) and the guidelines from the American Epilepsy society (62).

Stage two involves measuring performance. For comparison of current quality of care against set standards, each criterion has to have a pre-set performance threshold. A performance threshold/level of performance is a defined level or degree of expected compliance normally expressed as a percentage (60). The key factors considered when setting performance threshold are clinical importance, acceptability and practicability. A criterion whereby clinical importance is critical, for instance, safe use of AEDs will have a 100% threshold. However, practicability is considered in situations whereby clinical importance is not significant. This relates to a lower threshold being set due to limitations on resources. Acceptability relates to setting of optimum performance thresholds based on identification of level of care provided relating to the available resources and normal conditions for delivery of care. In addition, this stage entails data collection, data analysis and interpretation of audit results.

Stage 3 and 4 entail making and sustaining improvements. After obtaining audit results, areas with excellent delivery of care are acknowledged and no further re-audits are required. Also, areas that need improvement are identified and time-specific quality improvement plans are made to ensure that set standards are adhered to. Afterwards, a scheduled re-audit should be done to check if sustainable improvements have been made. To note, the audit cycle is a continuous process and audit tools developed need to be modified to suit current audit period.

For a clinical audit to be successful, involvement of stakeholders is crucial. In this audit, the key stakeholders will be involved in collection of audit data by giving suggestions/explanations of current practice findings and contributing to implementation of planned actions. They include health care workers involved in delivery of care, patients who are recipients of care as well as the hospital administration authorised in implementation of quality improvement areas of non-compliance.

2.4.2 Other Clinical Audits on Seizure management.

In the United Kingdom, a nationwide clinical audit was conducted focusing on management and care of children and young people with epilepsy (64). The audit aimed to identify areas for improvement and highlight best practices in Epilepsy management. The main areas that were audited were diagnosis and assessment, antiepileptic prescribing practices, Epilepsy management plans, transition to adult services, seizure management and emergency care, quality of life and patient outcome and transition to adult services. The audit started in 2012 consisting of four cohorts. The findings of the three cohorts were similar. The major area of improvement has been decreased use of Sodium valproate in females greater than 9 years. (65). Most of the criteria used for this audit are adopted from this clinical audit.

In Egypt, a clinical audit on management of childhood epilepsy was conducted at a tertiary children's hospital (74). The main criteria examined were on diagnosis and treatment. The main aim was to establish the most common diagnosis pathway used and most prescribed antiepileptics used in monotherapy and combination therapy. Similarly, diagnosis and treatment practices are examined in this audit.

In Kenya, there were no studies found on any clinical audit conducted on any seizure disorder/ Epilepsy management in the hospital setting.

2.4.3 Conceptual framework of acute seizure management

There are various causes of febrile seizures and acute symptomatic seizures. Acute seizure management is dependent on the causes of febrile seizures and acute symptomatic seizures. In addition, structural features and processes done influence whether there is seizure control or recurrence in acute seizure management. Figure 3 outlines how these variables influence acute seizure management.

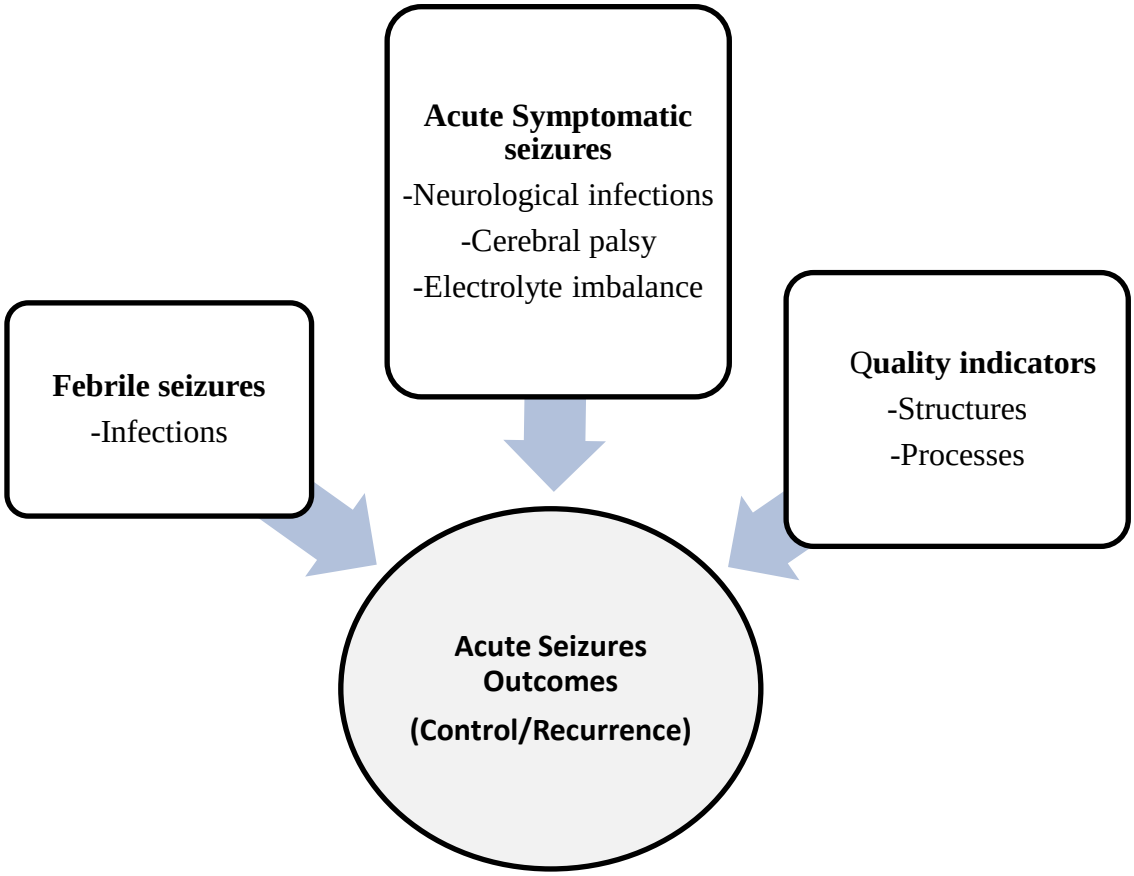


Figure 3: Conceptual framework of acute seizure management

CHAPTER THREE: METHODS

3.1 Study design

A descriptive cross-sectional study was done to find out the characteristics, management, and treatment outcomes of acute seizures among paediatric inpatients at KNH.

A clinical audit was also conducted to assess the structure, processes, and outcomes of acute seizure management of paediatric inpatients at KNH. An audit tool was developed (*Appendix B)* consisting of six sections.

3.2 Study site

Kenyatta National Hospital is a national tertiary referral and teaching hospital. It is located in Upper hill, 4 kilometres from the central business district in Nairobi, Kenya. The hospital has 50 wards, 22 outpatient clinics, 24 theatres and an accident and emergency department. The hospital has a bed capacity of 1800. Hence, it is appropriate to conduct this study at Kenyatta National Hospital general medical Paediatric wards: 3A, 3B, 3C, 3D and Paediatric specialized unit. The general wards have a bed capacity of 256 beds often with over 100% bed occupancy. The paediatric specialized unit deals with patients requiring intensive care services. Being a referral tertiary hospital, it offers emergency, inpatient and outpatient services to a diverse number of patients referred from across the country and has the capacity to manage various seizure disorders and epilepsy syndromes, which made it a very suitable site for this study.

3.3 Study period

The study period for the clinical audit was between December 2020 and January 2021. Patient records included for the cross-sectional study was from December 2019 to January 2021.

3.4 Cross-Sectional Study

3.4.1 Study population

The study population was paediatric patients aged between 1 month and 5 years admitted to the paediatric wards (wards 3A, 3B, 3C, 3D) and paediatric specialized unit with acute seizures.

3.4.2 Inclusion criteria

1) Inpatient children aged between 1 month and 5 years admitted with acute seizure during the study period December 2019 to January 2021.

3.4.3 Exclusion criteria

1) Children with other seizure disorders other than acute seizures.
2) Files with incomplete information

3.4.4 Sampling

3.4.4.1 Sample size calculation

Fischer's formula (66) was used to estimate the sample size for the descriptive cross sectional study based on the expected prevalence of acute seizures in paediatrics at KNH. In a study conducted in Kilifi, Kenya, the prevalence of acute seizures was found to be 6.1% in 2018 (19). Hence, the sample size estimation was calculated as follows:

$$n = \frac{Z^2 \times P(1-P)}{d^2}$$

Where;

n= sample size

P = estimated prevalence or proportion in the population

Z= 1.96 which is Z-value corresponding to a significance level of 0.05

d= 0.05 which is the desired degree of accuracy for the study

$$n = \frac{1.96^2 \times 0.061(1-0.061)}{0.05^2}$$

n = 88

To account for incomplete or missing data from the medical records, the sample size was adjusted upwards by 10%. Hence, for this arm of the study, the estimated sample size was 97.

3.4.4.2 Sampling procedure

Consecutive sampling was done. This was to ensure that the most current and relevant patient records were sampled for the study.

Records for each month were retrieved, starting with the most recent month. The records were then reviewed, and eligible records included until the sample size was achieved.

3.4.5 Data collection

For the cross-sectional arm of the study, data extraction form was used for data collection (*Appendix A*). Data was obtained from patient records from December 2019 to January 2021.

3.4.6 Data Analysis

Data entry and analysis was done using Microsoft Excel (2016) and STATA version 16 (StataCorp, USA) software packages respectively.

For specific objectives 1 and 2, descriptive data analysis was used to summarize the data such as mean (standard deviation) and median (ranges) for continuous variables such as age and weight, and proportion and percentages for categorical variables such as acute seizure type and antiepileptic use. The Shapiro-Wilk test was used as a test for normality.

Graphic and tabular data presentation was used for quantitative data, accompanied by a narrative description.

3.5 Clinical Audit

3.5.1 Development of the Clinical audit tool

The clinical audit tool (*Appendix B*) was put together through consolidation of information from various sources. This included the Kenya National Guideline for Management of Epilepsy, the Basic Paediatric Protocol and the KNH formulary. In support of evidence-based practice, the NICE Guidance 27 for Epilepsy in children and young people (2013) (61) and the guidelines from the American Epilepsy society (62) were used to formulate the tool. Other audits used as reference are Epilepsy12 audit carried out in the United Kingdom in children and young people with epilepsy (https://www.rcpch.ac.uk/work-we-do/quality-improvement-patient-safety/epilepsy12-audit), the National Audit of Seizure management in hospitals (NASH) (http://www.nashstudy.org.uk) and the NHS Clinical Audit Policy (67). Table 4 outlines the sources of data used for the six sections included in the audit tool.

Table 4: Sources of data adopted for the audit tool

Sections of clinical audit tool	**Sources of Data**
Section 1: General Information	NHS Clinical Audit Policy
Section 2: Standards for Antiepileptic use in paediatric in-patients	the NICE Guidance 27 for Epilepsy in children and young people, guidelines from the American Epilepsy society, Kenya National Guideline for Management of Epilepsy, the Basic Paediatric Protocol and the KNH formulary
Section 3: Audit data collection tool	
Criterion 1: Structural features	the NICE Guidance 27 for Epilepsy in children and young people
Criterion 2: Appropriate and competent staff	Kenya National Guideline for Management of Epilepsy, the KNH formulary
Criterion 3: Appropriate assessment, classification and Investigations	Kenya National Guideline for Management of Epilepsy, the Basic Paediatric Protocol and the KNH formulary
Criterion 4: Safe and Effective use of Antiepileptics	Kenya National Guideline for Management of Epilepsy, the Basic Paediatric Protocol and the KNH formulary
Criterion 5: Patient satisfaction and clinical outcome	Epilepsy12 audit and the National Audit of Seizure management in hospitals (NASH)
Section 4: Criterion scoring summary sheet	NHS Clinical Audit Policy
Section 5: Assessment of criterion per standard set	NHS Clinical Audit Policy
Section 6: Quality improvement action plan	NHS Clinical Audit Policy

3.5. 2 Structure and sections of the clinical audit tool

The clinical audit tool (*Appendix B*) is made up of six sections, each with a specific purpose.

Section 1: This section collects data about the facility where the audit is carried out, the audit date/period and the department/ward involved. Also, where applicable, patient or HCW code number is included. In summary, this section describes where, when and by whom the audit is carried out. Following this, is a short introduction and description of the tool.

Section 2: This section gives a description of the standards for acute seizure management in paediatric in-patients, by which the clinical audit findings are compared.

Section 3: This section includes the data collection segment of the audit tool. There are five main criteria (described in section 3.5.3) each with a series of targeted questions. Each question is given a score that is used to calculate level of compliance.

Section 4: This section guides on how scoring of criteria is done. A scoring table is used in calculation of each criterion. In addition, an overall score is obtained from summation of actual score divided by the total expected score and given as a percentage.

Section 5: In this section, each criterion is assessed as per set level of performance.

Section 6: In this section, a Quality Improvement Action Plan template is illustrated. Areas of non-compliance are pointed out and relevant action advised for improvement of quality-of-care services. In future re-audits, areas of non-compliance can be investigated to check if sustainable improvement has been achieved

3.5.3 Criteria for audit

Criterion 1: Structural features

This criterion assessed if there were adequate structural features to facilitate safe and effective use of AEDs in seizure management. The key features examined were availability of specific AEDs at the hospital, access and availability of guidelines, protocols and policies governing seizure management, availability of various healthcare workers at the facility and the availability and access of functioning resuscitation equipment at the wards.

Four specific questions were used to source data for this criterion as described in Section 3, Appendix B.

Criterion 2: Appropriate and Competent staff

This criterion evaluated the adequacy of human capacity in seizure management at the hospital. It assessed the competency of various HCWs at various stages of provision of care based on cadre, years of practice and specified authorised duties in seizure management i.e., diagnosis, prescribing, dispensing, administration, monitoring and patient education. Also, the awareness of availability and use of guidelines/policies and protocols was assessed.

For this criterion, HCWs were interviewed as described in section 3, Appendix B using five specific questions.

Criterion 3: Appropriate assessment, classification and investigations

This criterion evaluated how the diagnosing process of acute seizures was carried out. Specific HCWs were asked what basis led to the acute seizure diagnosis, if any laboratory investigations were done and the appropriateness of the diagnosis.

For this criterion, four specific questions were used to source data as described in section 3, Appendix B.

Criterion 4: safe and effective use of AEDs

This criterion assessed if appropriate precautions and considerations were done during various processes of seizure management. i.e., prescribing, dispensing, administration and monitoring. The appropriateness of the AED regimen to the acute seizure type was checked as well as the initiation and withdrawal of AEDs. Additionally, it was noted if monitoring of drug toxicity and drug interactions were done.

For this criterion, six questions were used to source for data via observation of processes and patient files as described in section 3, Appendix B.

Criterion 5: patient satisfaction and clinical outcome

This criterion evaluated the satisfaction levels of the patient to the quality of care provided during the period of hospitalisation. In addition, if the seizures were adequately controlled or not, as well as any reported adverse effects following AED use.

For this criterion, five questions were used to source for data via interviews of caregivers and patient files as described in section 3, Appendix B.

3.5.4 Performance thresholds/Standards of Audit Criteria

A performance threshold/level of performance is a defined level or degree of expected compliance normally expressed as a percentage (60). The key factors considered when setting performance threshold are clinical importance, acceptability and practicability. A criterion whereby clinical importance is critical, for instance, safe use of AEDs will have a 100% threshold implying full compliance to set standards and must be achieved for quality of care to be considered appropriate. However, practicability is considered in situations whereby clinical importance is not significant. This translates to a lower threshold being set. For example, patient satisfaction to quality of care provided is subjective, hence its threshold for full compliance is set at 80% as this is sufficient and is not very important clinically.

A summary of the standard/performance thresholds set for this clinical audit is shown in Table 5. A similar table is included in the audit tool (*Section 2, Appendix B*).

Table 5: Standards for antiepileptic use in paediatric in-patients at KNH

	CRITERION	PERFOMANCE THRESHOLD (%)	DESCRIPTION
1	In the facility, adequate structural features are available and accessible for seizure management	100%	Adequate staff, medication, resuscitation equipment should be accessible and available at the facility
2	There are appropriate and competent personnel trained in seizure management	100%	To minimize errors and improve health outcomes, competent staff should have relevant skills and training
3	Appropriate assessment, classification and investigations of Acute seizures are done	100%	Diagnosis of acute seizures should be based on relevant guidelines
4	Procedures and precautions regarding prescribing, dispensing, administration, monitoring and patient education are done	100%	Processes relating to prescribing, dispensing, administration, monitoring of AEDs and patient education should be done according to set guidelines
5	Patients are satisfied with quality of care offered by the facility and resolution of acute seizures	80%	Patient satisfaction is subjective and resolution/recurrence of acute seizures is dependent on certain factors

Figure 4 below shows the key interpretation of levels of performance as adopted from NICE guidance audit (64).

Performance threshold at 100%

Full compliance	Partial compliance	Non- compliance
90-100%	70-89%	< 69%

Performance threshold at 80%

Full compliance	Partial compliance	Non- compliance
70-80%	51-69%	< 50%

Figure 4: Interpretation of the Level of Compliance with the set Performance Threshold

3.5.5 Data Collection using the Clinical Audit Tool

In each of the criterion, there were different sources of data from which data was collected as described below.

1. **Structural audit**

   Systems information such as staffing and training were obtained from the health information and records department as well as the human resource department. Physical checks were done for determination of availability and access of antiepileptics at the pharmacy and resuscitation equipment at the wards.

2. **Process audit**

   Processes refer to the activities that together constitute the care pathway of seizure management (prescribing, dispensing, administration and monitoring). For the audit of these processes, direct observation was done. Also, interviews of relevant health care workers and caregivers was done during or after processes were carried out. Review of patients' medical records were also used to supplement information on processes such as diagnosis. In this study, informed consent (*Appendix C*) was sought from care givers before any data collection was carried out. According to the NHS guidelines on clinical audits (68), a sample of 20-50 patients is sufficient to measure if standards are being followed. Hence, a minimum of 20 patients is considered adequate. This 'snapshot'sample should allow for rapid data collection that is representative of the audit population during the audit period. Therefore, for this audit, 34 healthcare workers from different cadres were interviewed together with 20 care givers.

3. **Outcome audit**

   Data on clinical outcome, for example resolution/recurrence of acute seizures was obtained from the patients' medical records. Information on patient satisfaction was also obtained by questioning the caregiver after each process (diagnosis, prescription, administration and monitoring) was carried out.

3.5.6 Analysis of the audit data

Data Analysis of the clinical audit data involved scoring of each criterion and presented in a criterion summary score sheet (*section 4, Appendix B*).

In each criterion, all the questions were equally weighted in the criterion and given a total score of ten. When scoring, a Yes was given a ten and a No given a zero. An Actual criterion score (AC) which was the total summation of all the 'Yes' scores was done for each criterion. A maximum criterion score (MC) was calculated as the total number of questions multiplied by ten for each criterion. The Criterion score was then calculated as a percentage using the following formula:

Criterion score (%) = (AC/MC * 100)

Thereafter, the Overall audit score will be calculated as:

Overall audit = (Σ AC/ ΣMC) * 100

Questions with no 'Yes or No' answer were included but not scored to allow for certain data collection for interpretation of audit results. This included criterion 2 investigating the cadres of the staff and the processes done by specific cadres. In criterion 3, more information was collected on how diagnosis was made.

The results obtained for each criterion was compared to pre-set standards for each criterion as described in *Section 5, Appendix B.*A criterion is an explicit statement that clearly defines what is being measured and represents important aspects of quality of care that can be measured objectively. A pre-set standard is a level or degree of expected compliance normally expressed as a percentage.

3.5.7 Quality Improvement Plan

A quality improvement plan was generated with guidance from the NHS Clinical audit policy (67) and practical guide to clinical audit (69). It included recommendations and responsible persons for each action plan for each area of non-compliance for each criterion.

3.6 Data Management and Quality Assurance

Patient identifiers were used instead of patient names. All data collection tools were stored safely under lock and key by the investigator. Electronic data was stored in password protected files and backed up regularly. This minimized loss and tampering of data.

Prior to data collection, the research assistant, who was a pharmacist intern at the hospital was briefed on what the clinical audit was about as well as trained on good data collection practices by the principal investigator. Emphasis was made on ensuring collection of complete data that

was accurate and consistent. The principal investigator ensured that the data collection process was done in a timely manner.

3.7 Ethical Considerations

Ethical approval to carry out the study involving human subjects and patient records was sought and obtained from Kenyatta National Hospital- University of Nairobi (KNH – UoN) Ethics and Research Committee (Ref No. P981/12/2019, Appendix F). Also, before conducting the audit, permission to conduct the audit was sought from KNH Research Office (Ref No. Paediatrics/232/2020, Appendix G). For the clinical audit section of the study, informed consent from the parent/guardian was sought in writing from patients after detailed explanation of the study.

3.8 Dissemination plan

Final copies of the thesis will be submitted to the medical library of the University of Nairobi and the Department of Pharmacy library for access by other students and university staff. A copy will be handed to the KNH research department as well as presentation of the study report via the KNH research journal club.

CHAPTER FOUR: RESULTS

For the clinical audit, data has been summarized in the format described in the audit tool. Descriptive statistics was used to analyse data for the cross-sectional part of the study. Frequency distribution tables, graphs and pie charts were used to aid in data visualization.

4.1 Cross Sectional Study

In this section, results obtained from the cross-sectional study describe the characteristics of in-patient paediatric patients with acute seizures.

4.1.1 Demographic findings

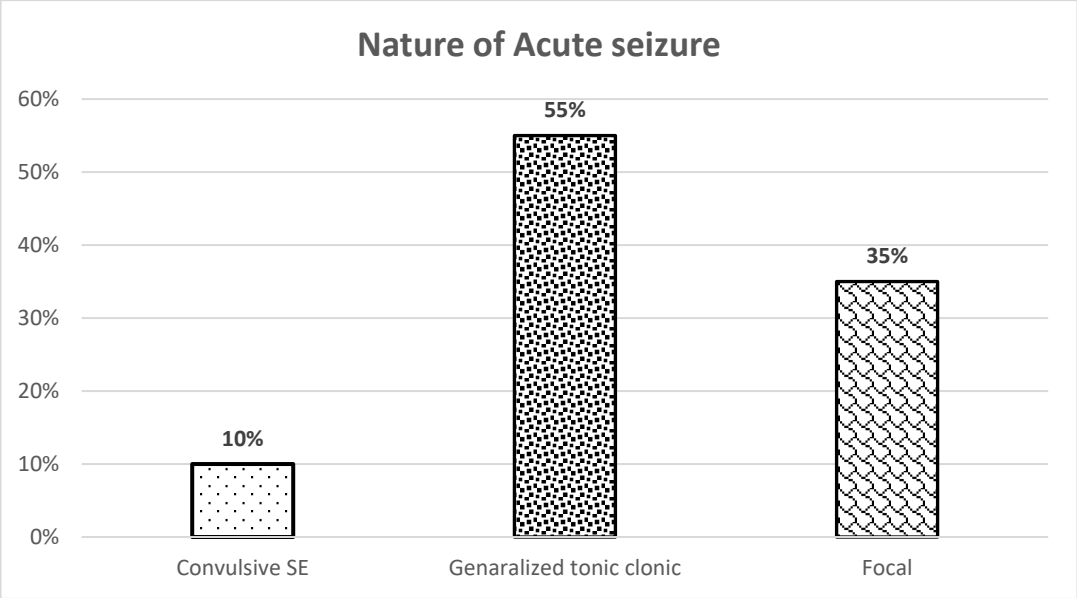
A total of 97 patient records were retrieved, data extracted and entered into the data extraction form (*Appendix A*). The minimum target sample size of 97 patient records was achieved. Most of the patients sampled were between ages 1 and 4 years and there were more males than females between with an average weight of 11 kgs, as shown in Table 5.

Table 5: Demographic characteristics of paediatric patients with acute seizures

	Mean (SD)	**Median (IQR)**
Demographics		
Age (yr.)		2 [1,4]
Weight (kg)	11.2 (5.0)	
Sex	**F**	**(%)**
Male	54	54
Female	43	44

4.1.2 Type of acute seizures

Most patients had FS 56 (58%) compared to ASS 41 (42%). Furthermore, majority of the patients experienced acute seizures that were generalized tonic clonic in nature. This was followed by focal seizures involving one body part. Convulsive status epilepticus was observed in 10 (10%) of the patients. It was the least common but most fatal, hence required critical management. This is demonstrated by Figure 5 which shows the nature of acute seizures recorded.



SE: status epilepticus

Figure 5: Nature of Acute Seizures

4.1.3 Causes of Acute seizures

The most common cause of acute seizure was meningitis linked to bacterial infection. Following, most patients had pneumonia that was caused by aspiration or *S. pneumoniae.* Also, gastroenteritis and tonsillitis contributed to a number of acute seizure cases. Other causes were cerebral palsy, rickets, malaria, and electrolyte imbalances. Table 6 shows the frequency of the causes of acute seizures that were recorded.

Table 6: Causes of Acute seizures

Causes	**F**	**%**
Bacterial meningitis	39	41
Pneumonia	27	28
Gastroenteritis	15	15
Tonsillitis	10	10
*Others	6	6

*Others: cerebral palsy, rickets, malaria, and electrolyte imbalances

4.1.4 Antiepileptic drug use

It was noted that 18 (19%) of AS did not require use of AEDs as symptomatic management was done such as antipyretic use for fever and antibiotics for infection. This is in line with recommendations by the Kenya National Guidelines for the Management of Epilepsy (3).The other 79 (81%) of AS required management with AEDs due to recurrent and or prolonged seizures. Most of the acute seizures required monotherapy using a single agent of AED for seizure management. As shown in table 7, the most common AED used for initiation and maintenance dosing either as monotherapy or combination therapy was Phenobarbital. This coincides with data showing the most frequent acute seizure type to be generalized seizures as Phenobarbital is one of the recommended AEDs for seizure control. Sodium valproate was frequently used for maintenance dosing as it is recommended for use in most of the seizure types. It was noted that Phenytoin and Diazepam were seldom used due to unavailability at the hospital pharmacy**.** Other AEDs available but less commonly used were oral Carbamazepine, Clonazepam and Lamotrigine. Table 7 shows initial and maintenance dosing of antiepileptics during acute seizure management at the hospital.

For management of complex seizures and convulsive status epilepticus, combination therapy was used. The most common combination therapy during initiation included Phenobarbital and Diazepam while a combination of Phenobarbital and Sodium valproate was frequently used during maintenance dosing.

Table 7: Initial and maintenance dosing of Antiepileptics

AED use	**F**	**%**
None	18	19%
Monotherapy/Combination therapy	79	81%
Total	97	100%
Initial dosing		
Monotherapy		
Phenobarbital	39	49%
Phenytoin	13	16%
Diazepam	7	9%
Combination therapy		
Phenobarbital+Diazepam	9	11%
Phenobarbital+Phenytoin	6	8%
Diazepam+Phenytoin	3	4%
Phenytoin/+Phenobarbital/+Diazepam+*Anaesthesia	2	3%
Total	79	100%
Maintenance dosing		
Monotherapy		
Phenobarbital	27	34%
Sodium valproate	11	14%
Phenytoin	3	4%
Combination therapy		
Phenobarbital+Sodium valproate	23	29%
Phenobarbital+Phenytoin	4	5%
Phenobarbital+Diazepam	5	6%
Phenobarbital/+Phenytoin/+Sodium Valproate+*Others	6	8%
Total	79	100%

*Others: Clonazepam, Lamotrigine, Carbamazepine * Anaesthesia: Propofol, Ketamine, Midazolam

4.1.5 Antiepileptic drug dosing

AED dosing was based on the weight of the patient. It was noted that for particular AEDs such as Phenobarbital and Phenytoin, a higher dose per kilogram was given in paediatrics than adults. This is because paediatric patients metabolize these drugs faster than adults.

Most of the patient records had correct dosing of the AEDs prescribed. However, four of the patient records had wrong doses that were prescribed and administered for a number of days. This was then stopped, and correct doses prescribed by a different prescriber and administered. It was noted that all the four patient records were corrected for their prescribing errors and dispensed accordingly.

4.1.6 Acute seizure control/recurrence

Majority of the patients had their seizures under control 70 (72%) following treatment after hospitalisation. However, 27 (28%) of the patients had recurrent seizures due to other comorbidities that had not been managed. For example, recurrent seizures due to infections such as tonsillitis required tonsillectomy for seizure resolution.

4.1.7 Lab monitoring, Adverse drug reactions and drug-drug interactions

Various AEDs have notable signs of toxicity from administration errors or dosing errors. Importantly, when administrating Phenytoin, Diazepam and Phenobarbital it was required that slow intravenous infusion be done. This is due to risk of cardiac arrythmias and hypotension hence cardiac and respiratory monitoring. In addition, access to resuscitation equipment was important in case of cardiac and respiratory related adverse effects.

It was noted that therapeutic drug monitoring was not done for AEDs at the hospital. In addition, though expected physical manifestations of adverse drug reactions such as somnolence with Phenobarbital and fainting with rapid Phenytoin infusion could be used for monitoring drug toxicity, they were not recorded in the patient files. Therefore, this indicates a gap in monitoring and recording of adverse drug reactions. From patient records, it was observed that drug-drug interactions were not checked. Most AEDs have drug-drug interactions with other AEDs. Dose adjustments may have to be made when a combination of AEDs is included in the same regimen. Using the online utility https://www.drugs.com/, the interactions within AEDs are classified as major, moderate and minor and are summarized in

Appendix D which shows the AED-AED drug interaction classification matrix. Also, interactions with other drugs and food can be checked on the same website.

Major drug interactions involving AEDs are highly clinically significant. This combination should be avoided as the risks outweigh the benefits. For major AED-AED interactions, it was noted that in very few instances, for poorly controlled seizures, patients were given more than two AEDs which included Sodium valproate and Lamotrigine. Notably, there is major interaction between Lamotrigine and Sodium Valproate. The risk of this drug combination outweighs the benefits. In children, Lamotrigine has a higher frequency of causing skin rashes. This is further exacerbated when it is co-administered with Sodium valproate and has a higher chance of causing Stevens–Johnson syndrome (SJS), which can be fatal**.** Fortunately, despite the risk, there were no records of any fatal outcome of the 6 patients who had this combination therapy as highlighted in Table 8.

Table 8: Potential drug interaction classification of different combination antiepileptic therapies

Combination antiepileptic drug therapy	**Patients on combination therapy**	**Potential Minor/Moderate/ Major drug Interactions**
Phenobarbital+Sodium valproate	23	Moderate
Phenobarbital+Diazepam	14	Moderate
Phenobarbital+Phenytoin	10	Moderate
Diazepam+Phenytoin	3	Moderate
Phenytoin/+Phenobarbital/+Diazepam+*Anaesthesia	2	Minor
Phenobarbital/+Phenytoin/+Sodium Valproate+*Others	6	Major: Sodium valproate+lamotigrine

*Others: Clonazepam, Lamotrigine, Carbamazepine * Anaesthesia: Propofol, Ketamine, Midazolam

Moderate drug interactions involving AEDs are moderately clinically significant and should be avoided unless under special circumstances. Most AED combinations with moderate drug interaction require dose adjustment due to their effects on drug metabolism. For instance, Phenytoin is a potent inducer of drug metabolizing enzymes and reduces the levels of drugs metabolized by these enzymes such as Topiramate and Sodium valproate. Hence, the need to reduce doses of these drugs. For maintenance doses, most patients had a combination of Phenobarbital and Sodium valproate. This requires lowering of Phenobarbital doses as Sodium valproate causes metabolic inhibition of Phenobarbital hence causing spiking of serum levels

of Phenobarbital (70). As shown in Table 8, most patients had combination therapies with moderate drug interactions. Patient files had no recording of whether dose adjustments were done despite the risk of their pharmacokinetic interactions.

4.2 Clinical audit

The main objective of conducting this clinical audit was to examine the characteristics, management and outcome of acute seizure in paediatric patients at KNH. An audit tool was developed to examine the structures, processes and outcome that characterize acute seizure management at KNH.

4.2.1 Clinical Audit of Acute seizure management at KNH

The clinical audit tool developed in Appendix B was used to conduct the audit of acute seizure management at KNH

4.2.1.1 Collection of Audit data and Audit results

Data for each criterion was collected using the audit tool. Relevant data sources were used in data collection.

Criterion 1: Structural features

Sources of data for the structural features were obtained from the health information and records department and physical checks at the pharmacy and wards.

It was observed that there are guidelines, protocols and policies in place for seizure management. These were easily available and accessible in print and digital formats. It was noted that there was adequate number of various cadres of healthcare workers in the facility serving in various capacities and with varied levels of work experience. All the wards included in the study had easy access and availability to fully functioning resuscitation equipment. During the period of the audit, most of the essential AEDs were available with exception of Diazepam in the per rectal and Intravenous formulations. Also, Phenytoin syrup was out of stock.

This criterion had a 90% score showing full compliance for structural features required in management of acute seizures in paediatric patients. The only deficiency was full availability of essential AEDs in different formulations as stated previously.

Criterion 2: Appropriate and Competent staff

There were various HCWs available with varying years of practice. All of the different cadres used guidelines, protocols and policies as per their role in seizure management i.e., diagnosis, prescribing, dispensing, administration and monitoring. The guidelines, protocols and policies used included the KNH Formulary, Basic and paediatric protocols, hospital SOP on seizure management in paediatrics.

This criterion had a 100% score showing full compliance on having appropriate and competent staff.

Criterion 3: Appropriate assessment, classification and investigations

Observation and detailed history were used as basis of diagnosis of AS. In addition, laboratory investigations were carried out to aid in finding out the causes of AS and knowing the AS phenotype for appropriate management. These included full haemogram, Urea, Electrolyte, Creatinine tests, Liver Function tests, CT and MRI scans, CSF testing, malaria slide etc. This criterion had a 100% score showing full compliance on having appropriate assessment, classification and investigations.

Criterion 4: Safe and Effective use of AEDs

Sources of data on safe and effective use of AEDs were obtained from observation of processes such as prescribing, dispensing, administration and monitoring as well as patient files. There were ten different AED regimens prescribed and (9) 90% of the AED regimens being appropriate to the diagnosis with resolution of seizures. However, there were four inappropriate prescriptions that were done by junior prescribers and corrected by senior prescribers after a couple of days upon review. Some of the inappropriate AEDs had already been administered and stopped when the correct AED regimen was initiated and administered.

It was noted that laboratory monitoring of AED plasma levels was not a routinely done activity at the hospital. Mostly, lack of monitoring was reported to be due to the costly nature of the activity. However, adverse drug reactions were monitored via known observable side effects such as somnolence signifying phenobarbital overdose, fainting with rapid infusion of Phenytoin etc but not recorded in patient files.

Notably, in 2018, there were various reports received at the hospitals' pharmacovigilance department of adverse effects following intravenous Phenytoin administration. This was due

to administration error of rapid intravenous infusion leading to hypotension in patients thus fainting. Subsequently, a short training was conducted targeting nurses and there have been no reports associated with this administration error. In addition, the importance on correct reconstitution of intravenous phenytoin was emphasized. This included, ensuring that reconstitution is not made with glucose containing solutions and administration of the drug within one hour to avoid precipitation of the solution due to crystallization.

This criterion had a 60% score showing non-compliance on safe and effective use of AEDs. The major shortcomings were lack of monitoring for drug toxicity and checking for drug interactions when using AEDs.

Criterion 5: Patient satisfaction and clinical outcome

Caregivers to the patients expressed their level of satisfaction with (13) 65% stating that they were satisfied with the level of quality of care received. However, (7) 35% stated that they were not satisfied with a scenario where they were required to buy medicine that was out of stock or outsource a laboratory test, for example, scans. Most patients' seizures were controlled with few seizures that were not well controlled due to various factors such as other co-morbidities not well managed or an out-of-stock drug not administered or awaiting proper diagnosis with pending lab tests that needed to be outsourced such as scans.

This criterion had a 60% score showing partial compliance on patient satisfaction and clinical outcome. Mainly, the limitations were on level of patient satisfaction with the quality of care provided due to stock outs or delays as described previously. Also, the care givers stated they were not counselled on how to administer first aid during acute seizure episodes, the signs and symptoms to look out for during an acute seizure manifestation and importance of compliance to prescribed AEDs.

4.2.1.2 Interpretation of audit results

The criterion score was obtained by adding up all the Yes answers and multiplying by 10. This was guided by the scoring criteria as described in Section 4, Appendix B. The summary of the scores per criterion is shown in Table 9. Table 10 shows the comparison of the audit findings with the pre-set performance threshold.

Table 9: Criterion Scoring sheet showing summary of the scores per criterion.

Criterion	Actual Criterion Score (AC)	Maximum Criterion Score (MC)=Total Number of Questions× Maximum Score (10)	Criterion Score as a percentage= (AC/MC×100)
1	90	100	90%
2	10	10	100%
3	20	20	100%
4	30	50	60%
5	30	50	60%

Overall audit = (∑ AC/ ∑MC) * 100 = (180/230) *100= 78%

Table 10: Assessment of criterion per standard set

	CRITERION	**PERFOMANCE THRESHOLD (%)**	**OBSERVED (%)**	**COMMENT**
1	In the facility, adequate structural features are available and accessible for seizure management	100%	**90%**	**There was full compliance to the performance threshold**
2	There are appropriate and competent personnel trained in seizure management	100%	**100%**	**There was full compliance to the performance threshold**
3	Appropriate assessment, classification and investigations of Acute seizures are done	100%	**100%**	**There was full compliance to the performance threshold**
4	Procedures and precautions regarding prescribing, dispensing, administration, monitoring and patient education are done	100%	**60%**	**There was non-compliance to the performance threshold**
5	Patients are satisfied with quality of care offered by the facility and resolution of acute seizures	80%	**60%**	**There was partial compliance to the performance threshold**

Criterion 4 had a 60% score showing non-compliance on safe and effective use of AEDs. The major shortcomings were lack of monitoring for drug toxicity and checking for drug interactions when using AEDs. Also, criterion 5 had a 60% score showing partial compliance on patient satisfaction and clinical outcome. Mainly, the limitations were on level of patient satisfaction with the quality of care provided due to stock outs or delays as described previously. Also, the care givers stated they were not counselled on how to administer first aid during acute seizure episodes, the signs and symptoms to look out for during an acute seizure manifestation and importance of compliance to prescribed AEDs.

CHAPTER FIVE: DISCUSSION, CONCLUSION, LIMITATIONS AND RECOMMENDATIONS

5.1 Discussion

The cross-sectional part of the study found that at KNH, most patients with acute seizures had febrile seizures 56 (58%) than acute symptomatic seizures 41 (42%). This is in contrast to a study done in Kilifi, Kenya that found the prevalence of ASS to be 3.2% and FS at 2.9%.This is because most patients had infections that caused neurological insult such as complicated Malaria (19).A study done in Tanzania found the prevalence of febrile seizures to be 2.1% and mainly caused by respiratory infections and malaria related with fever and gastroenteritis. (28).Globally, febrile seizures are experienced more than acute symptomatic seizures in children aged 1-5 years with a prevalence of 2-5%.In Western countries, most cases of febrile seizures are attributed to upper respiratory infections, *shigella* gastroenteritis, otitis media and human herpes-6 infections (roseola) (71).

It was found that 18 (19%) of patients with AS did not require AED use and were managed by treating the underlying causes and symptomatic management of the fever. This is in line with current guidance (3). Patients with recurring or prolonged AS were managed with AEDs as well as treatment of underlying comorbidities. The most common AEDs used for initiation and maintenance dosing was Phenobarbital as a monotherapy or in combination therapy. In contrast, a systematic review of published guidelines on management of acute seizures in children observed that Benzodiazepines were the first line in management of ongoing seizures. If two doses of Benzodiazepines failed, longer acting AEDs such as Phenytoin, Phenobarbital or Sodium valproate were indicated (72).

It was observed that 9 (90%) of the had correct diagnosis and classification of the acute seizure type and had the correct regimen and dosing. However, four prescriptions had wrong AED regimen and dosing errors done by junior prescribers. It was noted that these errors were corrected at later dates by senior prescribers and administered. It is acknowledged that children are at a higher risk of medication errors/prescribing errors due to weight-based dosing and human calculation errors. In a study assessing frequency of prescribing errors by junior prescribers, dosing errors of AEDs (Phenytoin, Phenobarbital, Carbamazepine and Sodium Valproate) were found to have most common prescribing error rates (73).It was noted that new paediatric intern prescribers and visiting prescribers had a higher prescribing error rate.

Another study showed that resident prescribers with increased repetition, practice and work experience had fewer prescription errors (74). It can be seen that KNH can reduce prescribing errors of AEDs by adopting various strategies such as prompt review of prescriptions by the pharmacy department and senior prescribers and provision of individual feedback and frequent continuous training of prescribers.

Recording of adverse drug reaction (ADR) was poorly done in patient files. Drug interactions and laboratory drug monitoring of AEDs was not a routinely done activity. This finding is reiterated by a study on antiepileptic drug toxicity in children that found that most clinical trials involving children with seizure disorders have minimal data records of safety profile in children (75) .There are various drugs known to interact with various AEDs and can be checked via https://www.drugs.com/. They are classified as Major, Moderate and Minor. In a cohort study conducted in the United Kingdom aimed at providing evidence of comparative toxicity of AEDs, it was found that monotherapy had less adverse effects than polytherapy (76).Hence, monotherapy should be considered whenever it is possible.

A clinical audit tool was developed and used to conduct a clinical audit of acute seizure management in paediatric patients at KNH.

Criterion 1 of the audit revealed that most structural features were compliant such as availability of resuscitation equipment, access and availability of guidelines and protocols on seizure management and there was adequate healthcare staff. However, availability of some essential AEDs during the period of the audit were out of stock such as Phenytoin syrup, Diazepam per rectal and intravenous formulations. This was an inconvenience to the caregivers that would force them to source the medicines outside the hospital.

Criterion 2 assessed if there were competent staff. It was observed that there were various cadres of HCWs with varying years of training, practice and expertise. This criterion was fully compliant. This is notable as it helps in service delivery to the patients as a wide array of health workers are available at the hospital.

Criterion 3 assessed the basis of diagnosis as per guidelines and protocols. Diagnosis of acute seizure was based on observation, history and lab investigations and fully compliant with guidelines and protocols. This is commendable as it aids in delivery of good quality of care to the patients.

Criterion 4 assessed the safe and effective use of AEDs. It was noted that this criterion had the most non-compliance. It was found that HCWs referenced the available guidelines and protocols as per recommendations. However, there were instances of medication errors in terms of wrong regimen or dosing errors done by junior prescribers that were later corrected by senior prescribers before dispensing. It was noted that laboratory monitoring of therapeutic drug levels was not routinely done at the hospital. Drug toxicity was mostly assessed through documented side effects of the AEDs. For example, somnolence with Phenobarbital signified overdose and fainting with Phenytoin signified rapid intravenous infusion during administration. In addition, checking of drug interactions was not a routine practice despite the patients being on various medications due to other co-morbidities. This is particularly concerning because there is a gap in monitoring of drug toxicity and drug interactions with AEDs which can negatively affect the wellbeing of patients.

A quality improvement plan was developed after the audit. The audit findings were shared with the paediatrics department and KNH Research department.

In Egypt, a clinical audit on management of childhood Epilepsy was conducted at a children's hospital (77), The main criteria examined were on diagnosis and treatment. It was observed that neuroimaging was commonly used for diagnosis. This is in contrast to KNH where patient history and observation were commonly used to aid in diagnosis. It was found that Carbamazepine and Sodium valproate were commonly used antiepileptics and administered as monotherapy. In KNH, Phenobarbital was mostly used in monotherapy and combination therapy.

In the United Kingdom, a nationwide clinical audit was conducted focusing on management and care of children and young people with Epilepsy. The audit aimed to identify areas for improvement and highlight best practices in Epilepsy management. The main areas that were audited were diagnosis and assessment, antiepileptic prescribing practices, Epilepsy management plans, transition to adult services, seizure management and emergency care, quality of life and patient outcome and transition to adult services. The audit started in 2012 consisting of four cohorts. The findings of the three cohorts are similar. The major area of improvement has been decreased use of Sodium valproate in females greater than 9 years. The current area that needs more improvement is individual care plan of the patient while in school. In comparison to the audit conducted in KNH, it was noted that seizure management in the United Kingdom is wholesome and quality of care of patients is taken into consideration from

school, home to the hospital setting. Pattern of use of Sodium valproate in girls greater than 9 years was not obtained as data for this clinical audit was obtained from children below five years. This can be considered in future audits. Sodium valproate should be used with caution in females of child bearing age due to its teratogenic adverse effects.

In Kenya, currently, there are no similar clinical audits done on management of seizure disorders and Epilepsy.

5.2 Study limitations

At the initial stages of observation of processes, there was risk of observer bias as HCWs observed may have behaved different than normal. However, with time, as the researcher became part of the team, observer bias was minimized.

Also, there was risk of response bias which was minimized by avoiding leading questions.

For the cross-sectional arm of the study, there was non-inclusion of patient records who were deceased as access to the patient files was restricted at the records department due to misfiling. This created a risk of selection bias.

The audit tool might have some gaps in scope and questions as this was the first version. Future versions would benefit from KNH staff and management feedback.

5.3 New Knowledge from the study

It has been noted that there are various causes of acute seizures in certain settings dependant on prevalence and incidence of certain illnesses. It was observed that pattern of Antiepileptic use is greatly influenced by availability of drug and the most seizure type observed. In addition, the level of control of acute seizures is greatly influenced by management of underlying condition.

5.4 Conclusion

The most common type of AS was determined to be FS. Among the most reported causes of AS at the hospital were bacterial meningitis, pneumonia (*S. pneumoniae* and aspiration) and gastroenteritis. AED use in management of AS was only done when the seizures were recurrent or prolonged. The frequently used AED was Phenobarbital as a single agent or in combination therapy. The clinical audit found that most of the criterion related to structures, processes and outcome of acute seizure management to be compliant. However, major areas of non-

compliance were on correct dosing and prescribing of correct regimen of AED and availability of particular AEDs. According to caregivers, stock-outs caused inconveniences to the patient as they were required to buy the medication out of the hospital. If the medicine was not bought, it was not administered. This impacted poorly on seizure control.

The main objective of the study which was to examine the characteristics, management and treatment outcomes of acute seizure management was therefore achieved. The clinical audit and cross-sectional arm of the study established a major area of non-compliance regarding safe and effective use of AEDs. This was due to dosing errors, minimal checks for drug-drug interactions and monitoring of drug toxicity. A quality improvement plan was developed (see *Table 11, section 5.4)* and presented to the KNH research department.

5.5 Recommendations

5.5.1 Recommendations for practice

A summary of the critical gaps and recommendations are shown in the quality improvement plans shown in Table 11. The hospital management and specific department should try to implement all action plans where possible.

Table 11: Quality Improvement action plan

Criterion	Area of non-compliance	Corrective action to be taken	Responsible person
1	Some essential AEDs were out of stock, for example, Diazepam (per rectal and injection), Phenytoin syrup during the audit period.	The Pharmaceutical procurement and supply team should ensure Essential medicines are in stock at all times	Pharmaceutical procurement and supply team
2	Junior prescribers making medication errors when prescribing AEDs	Continuous education for junior prescribers to minimize medication errors with AED use	Senior prescribers in paediatric department
3	Laboratory drug monitoring not done	Hospital management should look for ways to incorporate laboratory drug monitoring services	Hospital management
4	Lack of routine checks for drug interactions and documentation of ADRs	All prescribers should improve on documentation and management of ADRs and routinely check for drug interactions	Prescribers in paediatric department
5	Patients inconvenienced by stock-outs	Hospital management should ensure there are minimal stock-outs	Hospital management

5.5.2 Recommendations for future research

It is reported that recurrent episodes of acute seizures increase the risk of developing epilepsy. Research should be done to establish how many patients convert to epilepsy after the first AS episode and the quality of care they received.

Research should be done on long term adverse effects of AEDs in children. Future audits can also be done on chronic management of other seizure disorders, Epilepsy and Epilepsy syndromes in paediatric and adult patients.

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APPENDICES

APPENDIX A: DATA EXTRACTION FORM FROM PATIENT RECORDS FOR THE CROSS-SECTIONAL ARM OF THE STUDY

Version June 2020

Serial No **Date of data collection**

A. BIODATA

1. Age: _____
2. Gender: M [ ] F [ ]
3. Weight:_____
4. Height:_____
5. BMI : _____
6. Residence:_____

B. PATIENT MEDICAL HISTORY AND CLINICAL CHARACTERISTICS

1. Admission Diagnosis: _____
2. Acute seizure type: _____
3. Co-morbidities: _____
   _____
   _____
4. Any additional relevant information: _____
   _____
   _____

C. CURRENT MEDICATION

Antiepileptic drugs

	AED	Date		Dose	Frequency	Duration	Route
		Started	Stopped				
1							
2							
3							
4							
5							
6							

Other drugs

	Drug	Date		Dose	Frequency	Duration	Route
		Started	Stopped				
1							
2							
3							
4							
5							
6							
7							
8							
9							
10							

D. REVIEW OF CURRENT THERAPY

1. Were any lab investigations done to aid in diagnosis? Yes [ ] No [ ]

2. If Yes to Q.1 please specify

3. Was initiation of AEDs appropriate? Yes [ ] No [ ]

4. Was withdrawal of AEDs appropriate? Yes [ ] No [ ]

5. If No to Q.3 and/or Q.4, briefly explain.

6. What was the level of seizure control? Recurrence [ ] Resolution [ ]
   Comment:

7. Was there any monitoring of drug toxicity carried out? Yes [ ] No [ ]

8. If Yes to Q.7 please specify

9. Were there any potentially serious drug interactions? Yes [ ] No [ ]

10. If Yes to Q. 9 please specify

11. Were there any adverse effects caused by AEDs? Yes [ ] No [ ]

12. If Yes to Q.11 please specify

13. Note any additional relevant information

APPENDIX B: CLINICAL AUDIT TOOL FOR ANTIEPILEPTIC USE IN PAEDIATRIC PATIENTS

Version 001 (June 2020)

SECTION 1: GENERAL INFORMATION

Facility Name and Code:	**Ward:**
Department/unit:	**Patient No/ HCW code no:**
Data collector (Clinical auditor):	**Audit date:**

This clinical audit tool consists of six sections. All sections should be duly filled.

This being the first version of this audit tool, there may be gaps in the scope and questions included. Therefore, feedback is encouraged on improvement of the audit tool and measurement plans **Feedback should be forwarded to the KNH research and programs department**

SECTION 2: STANDARDS FOR ANTIEPILEPTIC USE IN PAEDIATRIC IN-PATIENTS

A performance threshold/level of performance is a defined level or degree of expected compliance normally expressed as a percentage. It aids in measuring performance of a certain area highlighting compliance or non-compliance.

	CRITERION	**PERFOMANCE THRESHOLD (%)**	**DESCRIPTION**
1	In the facility, adequate structural features are available and accessible for seizure management	100%	Adequate staff, medication, resuscitation equipment should be accessible and available at the facility
2	There are appropriate and competent personnel trained in seizure management	100%	To minimize errors and improve health outcomes, competent staff should have relevant skills and training
3	Appropriate assessment, classification and investigations of Acute seizures are done	100%	Diagnosis of acute seizures should be based on relevant guidelines
4	Procedures and precautions regarding prescribing, dispensing, administration, monitoring and patient education are done	100%	Processes relating to prescribing, dispensing, administration, monitoring of AEDs and patient education should be done according to set guidelines
5	Patients are satisfied with quality of care offered by the facility and resolution of acute seizures	80%	Patient satisfaction is subjective and resolution/recurrence of acute seizures is dependent on certain factors

SECTION 3: AUDIT DATA COLLECTION TOOL

In this section, there are five criteria, each consisting of target questions to assess processes in seizure management in the institution.

Instructions:

- Use one clinical audit tool per patient/Healthcare worker
- Audit questions should be modified to the facility setting
- Some questions can be adjusted to suit individual requirements

CRITERION 1: STRUCTURAL FEATURES

This section examines adequacy of supporting features in the institution to enable effective seizure management

Sources of data and specific instruction: Data will be extracted from heath information and records department, human resource department and physical checks at the pharmacy and wards.

	QUESTION	**RESPONSE**
1.1	Are there guidelines, protocols and policies on Seizure management	Yes [ ] No [ ]
1.2	Are Antiepileptics available in the facility	Yes [ ] No [ ]
1.3	Are the following HCWs available in the facility	
	i. Consultants	Yes [ ] No [ ]
	ii. Medical officers	Yes [ ] No [ ]
	iii. Pharmacists	Yes [ ] No [ ]
	iv. Clinical officers	Yes [ ] No [ ]
	v. Nursing officers	Yes [ ] No [ ]
	vi. Pharmaceutical technologists	Yes [ ] No [ ]
	vii. Laboratory technologists	Yes [ ] No [ ]
1.4	Are resuscitation equipment available and accessible?	Yes [ ] No [ ]

Additional notes:

CRITERION 2: APPROPRIATE AND COMPETENT STAFF

This section examines if there are sufficient competent staff for delivery of care services in acute seizure management.

Sources of data and specific instruction: Information will be obtained from interviewing Healthcare workers. Relevant staff involved in the seizure management processes (assessment, prescribing, dispensing, administration and monitoring) will be interviewed .**Note:** One form for each staff interviewed.

	QUESTION	**RESPONSE**
2.1	What is your cadre?	Consultant [ ] Medical officer [ ] Pharmacist [ ] Clinical officer [ ] Nursing officer [ ]Pharmaceutical technologist [ ] Laboratory technologist [ ] Intern _____ Other _____
2.2	How many years of practice?	< 5 years [ ] 5-10 years[ ] >10 years [ ]
2.3	Which speciality are you trained on in use of Antiepileptics?	Prescribing [ ] Dispensing [ ] Administration [ ] Monitoring [ ] Patient education [ ]
2.4	Do you use any guidelines, protocols and/or policies for use of antiepileptics?	Yes [ ] No [ ]
2.5	If yes in Q 2.4, please specify resources used	1) _____ 2) _____ 3) _____

Additional notes:

CRITERION 3: APPROPRIATE ASSESSMENT, CLASSIFICATION AND INVESTIGATIONS

Appropriate assessment and lab investigations should be done to ensure proper diagnosis of acute seizures is done.

Source of data and specific instruction: Interview of Healthcare workers and patient files will be sources of data

	QUESTION	**RESPONSE**
3.1	What is the basis of Acute seizure diagnosis	Observation [ ] History [ ] Other [ ]
3.2	Have laboratory investigations been carried out to aid in diagnosis?	Yes [ ] No [ ]
3.3	If Yes in Q. 3.2, which laboratory investigations have been carried out?	1) 2) 3)
3.4	Is the classification of the seizure type appropriate?	Yes [ ] No [ ]

Additional notes:

CRITERION 4: SAFE AND EFFECTIVE USE OF ANTIEPILEPTICS

Appropriate precautions and instructions should be done to ensure seizure management processes in prescribing, administration and monitoring are as per standards.

Source of data and specific instruction: Observation of processes and patient files will be sources of data

	QUESTION	**RESPONSE**
4.1	Is the Antiepileptic regimen appropriate?	Yes [ ] No [ ]
4.2	Is administration of the Antiepileptic regimen appropriate?	Yes [ ] No [ ]
4.3	Is monitoring of drug toxicity done?	Yes [ ] No [ ]
4.4	If Yes for Q 4.3, please specify	1) _____ 2) _____
4.4	Are drug interactions considered when administering antiepileptics?	Yes [ ] No [ ]
4.5	Are appropriate initiation/withdrawal protocols on antiepileptic use followed?	Yes [ ] No [ ]

Additional notes:

CRITERION 5: PATIENT SATISFACTION AND CLINICAL OUTCOME

Source of data and specific instruction: Data is obtained from Interviewing of patients and patient records

Note: One form to be used per patient

	QUESTION	**RESPONSE**
5.1	Are you satisfied with the quality of care provided?	Yes [ ] No [ ]
5.2	Have you as the care giver been counselled on first aid of acute seizures, signs and symptoms of acute seizure manifestation and importance of compliance to antiepileptics?	Yes [ ] No [ ]
5.3	After administration of antiepileptics, have the seizures resolved?	Yes [ ] No [ ]
5.4	Have you observed any adverse effects after initiation of antiepileptics?	Yes [ ] No [ ]
5.5	If Yes in Q 5.4, were there any investigations done to confirm if antiepileptics were the cause?	Yes [ ] No [ ]

Additional notes:

SECTION 4: CRITERION SCORING SUMMARY SHEET

Scoring instructions: Scores: Yes = 10, No = 0. A score of ten is assigned to every Yes answer and a score of zero to every No answer.

The Actual criterion score is the sum of all the Yes answers

Criterion	**Actual Criterion Score (AC)**	**Maximum Criterion Score (MC)=Total Number of Questions✕ Maximum Score (10)**	**Criterion Score as a percentage= (AC/MC✕100)**

Criterion score (%) = (AC/MC * 100)

Thereafter, the Overall audit score will be calculated as:

Overall audit = (∑ AC/ ∑MC)* 100

The guide below will aid in Interpretation of results as per NICE clinical audit policy.

Performance threshold at 100%

Full compliance	Partial compliance	Non- compliance
90-100%	70-89%	< 69%

Performance threshold at 80%

Full compliance	Partial compliance	Non- compliance
70-80%	51-69%	< 50%

Interpretation of the Level of Compliance with the set Performance Threshold

SECTION 5: ASSESSMENT OF CRITERION PER STANDARDS SET

	CRITERION	**PERFOMANCE THRESHOLD (%)**	**OBSERVED (%)**	**COMMENT**
1	In the facility, adequate structural features are available and accessible for seizure management	100%		
2	There are appropriate and competent personnel trained in seizure management	100%		
3	Appropriate assessment, classification and investigations of Acute seizures are done	100%		
4	Procedures and precautions regarding prescribing, dispensing, administration, monitoring and patient education are done	100%		
5	Patients are satisfied with quality of care offered by the facility and resolution of acute seizures	80%		

SECTION 6: QUALITY IMPROVEMENT ACTION PLAN

Criterion	Area of Non-compliance	Corrective action to be taken	Responsible person	Time frame	Review of Implementation action

APPENDIX C: PARTICIPANT INFORMATION AND CONSENT FORM -ENGLISH

STUDIES INVOLVING CHILDREN

PARENTAL CONSENT

Title of Study: CLINICAL AUDIT OF ACUTE SEIZURE MANAGEMENT OF PAEDIATRIC PATIENTS AT KENYATTA NATIONAL HOSPITAL

Principal Investigator \ and institutional affiliation: Faith Mwende Munyaysa, University of Nairobi

Co-Investigators and institutional affiliation: Dr Eric M. Guantai, University of Nairobi

Dr Kipruto A. Sinei, University of Nairobi

Dr Patrick Kivoto, Kenyatta National Hospital

Introduction:

I would like to tell you about a study being conducted by the above listed researchers. The purpose of this consent form is to give you the information you will need to help you decide whether or not your child should participate in the study. Feel free to ask any questions about the purpose of the research, what happens if your child participates in the study, the possible risks and benefits, the rights of your child as a volunteer, and anything else about the research or this form that is not clear. When we have answered all your questions to your satisfaction, you may decide if you want your child to be in the study or not. This process is called 'informed consent'. Once you understand and agree for your child to be in the study, I will request you to sign your name on this form. You should understand the general principles which apply to all participants in a medical research: i) Your child decision to participate is entirely voluntary ii) You child may withdraw from the study at any time without necessarily giving a reason for his/her withdrawal iii) Refusal to participate in the research will not affect the services your child is entitled to in this health facility or other facilities.

May I continue? YES / NO

For children below 18 years of age we give information about the study to parents or guardians. We will go over this information with you and you need to give permission in order for your child to participate in this study. We will give you a copy of this form for your records.

WHAT IS THE PURPOSE OF THE STUDY?

The researchers listed above are interviewing individuals who have acute seizures. The purpose of the interview is to find out if the hospital has offered adequate services to manage the condition. Participants in this research study will be asked questions about the quality of patient care delivered and if the condition has been well managed.

There will be approximately twenty participants in this study randomly chosen. We are asking for your consent to consider your child to participate in this study.

WHAT WILL HAPPEN IF YOU DECIDE YOU WANT YOUR CHILD TO BE IN THIS RESEARCH STUDY?

If you agree for your child to participate in this study, the following things will happen:

You will be interviewed by a trained interviewer in a private area where you feel comfortable answering questions. The interview will last approximately ten minutes. The interview will cover topics such as delivery of quality of care services and health outcomes.

ARE THERE ANY RISKS, HARMS, DISCOMFORTS ASSOCIATED WITH THIS STUDY

Medical research has the potential to introduce psychological, social, emotional and physical risks. Effort should always be put in place to minimize the risks. One potential risk of being in the study is loss of privacy. We will keep everything you tell us as confidential as possible. We will use a code number to identify your child in a password-protected computer database and will keep all of our paper records in a locked file cabinet. However, no system of protecting confidentiality can be absolutely secure so it is still possible that someone could find out your child was in this study and could find out information about your child.

Also, answering questions in the interview may be uncomfortable for you. If there are any questions you do not want to answer, you can skip them. You have the right to refuse the interview or any questions asked during the interview.

It may be embarrassing for you to have a child with acute seizures. We will do everything we can to ensure that this is done in private. Furthermore, all study staff and interviewers are professionals with special training in these examinations/interviews.

ARE THERE ANY BENEFITS BEING IN THIS STUDY?

Your child may benefit by receiving counselling on how to properly take medication, how to manage side effects and first aid during seizures etc. Also, the information you provide will help us better understand how to manage acute seizures. This information is a major contribution to science and the quality of care delivered by the hospital.

WILL BEING IN THIS STUDY COST YOU ANYTHING?

Being in this study will not cost you anything.

IS THERE REIMBURSEMENT FOR PARTICIPATING IN THIS STUDY?

There is no reimbursement for participating in this study.

WHAT IF YOU HAVE QUESTIONS IN FUTURE?

If you have further questions or concerns about your child participating in this study, please call or send a text message to the study staff at the number provided at the bottom of this page.

For more information about your child's rights as a research participant you may contact the Secretary/Chairperson, Kenyatta National Hospital-University of Nairobi Ethics and Research Committee Telephone No. 2726300 Ext. 44102 email uonknh_erc@uonbi.ac.ke.

The study staff will pay you back for your charges to these numbers if the call is for study-related communication.

WHAT ARE YOUR OTHER CHOICES?

Your decision to have your child participate in this research is voluntary. You are free to decline or withdraw participation of your child in the study at any time without injustice or loss of benefits.

Just inform the study staff and the participation of your child in the study will be stopped. You do not have to give reasons for withdrawing your child if you do not wish to do so. Withdrawal of your child from the study will not affect the services your child is otherwise entitled to in this health facility or other health facilities.

For more information contact:

1. **INVESTIGATOR**: Faith Mwende Munyasya **CONTACT:** 0715417876

2. **SUPERVISOR:** Dr E.M Guantai **CONTACT:** eguantai@uonbi.ac.ke
3. **SUPERVISOR:** Dr K.A Sinei **CONTACT:** sinei@uonbi.ac.ke
4. **SUPERVISOR:** Dr Patrick Kivoto **CONTACT:** wakivoto@gmail.com

5. **THE SECRETARY UON-KNH ETHICS AND RESEARCH COMMITTEE:**
   Prof. M.L. Chindia
   Postal Address: P.O Box, 19676-00202, Nairobi.
   Email address: uonknh_erc@uonbi.ac.ke **Telephone:** 2726300 Ext. 44102

CONSENT FORM (STATEMENT OF CONSENT)

The person being considered for this study is unable to consent for him/herself because he or she is a minor (a person less than 18 years of age). You are being asked to give your permission to include your child in this study.

Parent/guardian statement

I have read this consent form or had the information read to me. I have had the chance to discuss this research study with a study counsellor. I have had my questions answered by him or her in a language that I understand. The risks and benefits have been explained to me. I understand that I will be given a copy of this consent form after signing it. I understand that my participation and that of my child in this study is voluntary and that I may choose to withdraw at any time.

I understand that all efforts will be made to keep information regarding me and my child's personal identity confidential.

By signing this consent form, I have not given up my child's legal rights as a participant in this research study.

I voluntarily agree to my child's participation in this research study: Yes No

I agree to provide contact information for follow-up: Yes No

Parent/Guardian signature / Thumb stamp: _____ Date _____

Parent/Guardian printed name: _____

Researcher's statement

I, the undersigned, have fully explained the relevant details of this research study to the participant named above and believe that the participant has understood and has knowingly given his/her consent.

Printed Name: _____ Date: _____

Signature: _____

Role in the study: _____ [i.e. study staff who explained informed consent form.]

Witness Printed Name (If witness is necessary) _____

Signature: _____ Date; _____

FOMU YA KUIDHINISHA UTARATIBU WA KUKUSANYA UJUMBE NA

MAAFIKIANO -SWAHILI

Mada ya utafiti: Kudhibiti matibabu ya mshtuko kwa watoto kulingana na mikakati iliyowekwa katika hospitali kuu ya rufaa ya Kenyatta.

Tunakuomba ruhusa kwako ili ujisajili katika utafiti huu na mwanawe. Unafaa kuelewa mambo yafuatayo ya kimsingi yanayofaa kuzingatiwa na washiriki wote. Mwitikio wako wa kushiriki katika utafiti huu ni wa hiari. Unaweza kujitoa kutoka kwa utafiti huu wakati wowote pasipo kuhitajika kutoa sababu za kujitoa. Baada ya kusoma maelezo tafadhali, una uhuru wa kuuliza maswali yoyote yatakayokuwezesha kuelewa vizuri.

Naweza kuendelea? Ndio / Hapana

Utangulizi: Katika utafiti huu, nadhibitisha kama matibabu ya mshtuko kwa watoto wafanywa kulingana na mikakati iliyowekwa katika hospitali kuu ya rufaa ya Kenyatta.

Lengo la utafiti: Lengo la utafiti huu ni kujua ni katika daraja gani matibabu ya mshtuko kwa watoto haujafikia kiwango kinachohitajika. Mahala matibabu ya mshtuko ni nzuri patapelelezwa na umuhimu wake uhimizwe katika hospitali kuu ya rufaa ya Kenyatta.

Utaratibu: Kwa ruhusa yako, nitakushirikisha katika mjadala kuhusu maoni yako kuhusu jukumu lako katika matibabu ya mshtuko na vile umehitimu. Ujumbe wote utashughulikiwa kwa siri.

Hatari: Hakuna hatari yoyote kwako wala kwa mwanawe.

Faida: Majibu ya utafiti huu hautakusaidia wakati huu lakini utasaidia kuboresha matibabu ya wagonjwa wa mshtuko siku za usoni.

Hakikisho la usiri: Ujumbe wote utakaochukuliwa kwako utahifadhiwa kama siri. Hakuna wakati jina lako litatajwa au litumike wakati wa kuwasilisha ujumbe au kuandika nakala ya ujumbe gushi. Nambari za siri zitatumika.

Mawasiliano: Iwapo ungetaka kuwasiliana nami, ama maadili na kamati ambayo imeniruhusu kufanya utafiti huu, kuwa huru na utumie nambari za mawasiliano zilizoorodheshwa kwenye fomu hii.

1. **INVESTIGATOR**: Faith Mwende Munyasya **CONTACT:** 0715417876

2. **SUPERVISOR:** Dr E.M Guantai **CONTACT:** eguantai@uonbi.ac.ke

3. **SUPERVISOR:** Dr K.A Sinei **CONTACT:** sinei@uonbi.ac.ke

4. **SUPERVISOR:** Dr Patrick Kivoto **CONTACT:** wakivoto@gmail.com

5. **THE SECRETARY UON-KNH ETHICS AND RESEARCH COMMITTEE:**
   Prof. M.L. Chindia
   Postal Address: P.O Box, 19676-00202, Nairobi.
   Email address: uonknh_erc@uonbi.ac.ke **Telephone:** 2726300 Ext. 44102

FOMU YA IDHINI YA MSHIRIKI

Mimi niliyetia sahihi kwa hiari nakubali kushiriki utafiti huu na mtoto wangu. Nimeelezwa na kuelewa kinachohusiana na utafiti huu, majukumu yangu katika utafiti huu, athari zinazoweza kutokana na kujitolea kwangu na kuwa maswali yote yanayohusiana na utafiti huu nimeyajibu kama inavyotakikana. Naelewa kuwa naweza kuchagua kuacha kushiriki katika utafiti huu wakati wowote bila kupigwa penalti kwa njia yoyote. Naelewa kuwa ujumbe uliokusanywa utatumika kwa lengo la utafiti pekee na usiri wa hali ya juu utadumishwa.

Nitapokea nakala ya fomu hii iliyotiwa sahihi.

Jina la mlezi _____ sahihi _____ tarehe _____

MIADI YA MTAFITI

Nimeeleza ujumbe katika fomu hii kwa mshirika huyu na nimemtia moyo ili aulize maswali ambayo nitachukua wakati kuyajibu. Nimetosheleza kila mshirika kabisa na naelewa vipengee vyote vya utafiti kama ilivyoelezwa katika fomu ya kudhibitisha ruhusa hapo juu.

Jina la mtafiti_____sahihi_____Tarehe _____

Jukumu katika utafiti _____

Jina la mshahidi (kama ni lazima) _____ sahihi _____ Tarehe _____

APPENDIX D: ANTIEPILEPTIC-ANTIEPILEPTIC DRUG INTERACTION CLASSIFICATION

	Phenytoin	Phenobarbital	Diazepam*	Lamotrigine	Sodium valproate	Carbamazepine	Gabapentin	Pregabalin	Topiramate
Phenytoin									
Phenobarbital									
Diazepam									
Lamotrigine									
Sodium valproate									
Carbamazepine									
Gabapentin									
Pregabalin									
Topiramate									

*Same for Clonazepam and Lorazepam

No interaction	Minor	Moderate	Major

APPENDIX E: PHARMACOKINETIC PROFILE, ADVERSE EFFECTS AND DRUG INTERACTIONS OF ANTIEPILEPTIC DRUGS

AED	**SEIZURE TYPE**	**PK POFILE**						**DRUG INTERACTIONS**	**SIDE EFFECTS**	**PRECAUTIONS**
		Protein binding	**Half-life $t^{1/2}$**	**Absorption**	**Metabolism/ Elimination**	**Administration**	**Authority to prescribe at KNH**			
Phenytoin	Generalized tonic-clonic seizures, partial seizures	Highly protein bound	12-36	Formulation dependent	Dose dependent elimination No active metabolites	IV,PO *Tablets/Capsules* Phenytoin sodium 50mg,100mg *Oral solution(syrup)* Phenytoin sodium 30mg/5ml,100 ml bottle *Injection(solution for injection)*	*Essential Medicine Medical Officers(L_2) and above* *Essential medicine Medical Officers(L_2) and above*	Phenobarbital, carbamazepine, Sodium Valproate, Lamotrigrine, Isoniazid, felbamate, oxcarbazepine, topiramate, Haloperidol, Chlorpromazine, fluoxetine,	Diplopia, ataxia, gingival hyperplasia, hirsutism, neuropathy, sedation, agitation, gastric intolerance, blurred vision, ataxia, nystagamus, on IV	Precipitates with glucose solution IM not recommendedue to erratic absorption, precipitation at injection site and pain *Sign of drug toxicity:* Hyperglycaemia Slow IV infusion

						Phenytoin sodium 50mg/ml,5 ml ampoule	*Vital Medicine Medical Officers(L_2) and above*	fluconazole, digoxin, quinidine, cyclosporine, steroids, Alcohol,Methadone,Antacids, Amiodarone, Metronidazole, Clarithromycin,Ciprofloxacin,Isoniazid,Chloramphenical, cotrimoxazole, Rifamycin,MAoIs,TCAs,Mefloquine,Protease inhibitors etc	administration: cardiovascular and CNS depression with arrythmias (on rapid administration),hypotension	
Phenobarbital	Generalized tonic-clonic	Not significant	0.5-4 h (peak conc)		No active metabolites	IV,PO *Tablets(scored)* Phenobarbital 30mg	*Essential and*	Valproate, carbamazepine, felbamate,	Sedation, cognitive issues,	Avoid rapid IV administration and Intra-arterial adminstration

	seizures, partial seizures, myoclonic seizures, generalized seizures, neonatal seizures, status epilepticus	Protein binding	75-125(t1/2)			*Injection(concentrate solution for injection)* Phenobarbital sodium 200 mg/ml in propylene glycol 90% and water for injection 10%	*Restricted Medicine Medical Officers(L_2) and above* *Vital and Restricted Medicine Medical Officers(L_2) and above*	phenytoin, cyclosporine, felodipine, lamotrigine, nifedipine, nimodipine, steroids, theophylline, verapamil, Rifampicin, chloramphenicol, MAOIs, TCAs, Protease Inhibitors,Propranolol,CCBs, Corticosteroids,Theophylline,Montelurkast, vitamin D etc	ataxia, hyperactivity, mental depression, ataxia, paradoxical excitement, megaloblastic anaemia, osteomalacia, status epilepticus, hypotension, shock, laryngospasm, apnoea	*Signs of toxicity:* Hyperactivity and irritability in children Restlessness and confusion in elderly
Diazepam	Status epilepticus, seizure clusters	Highly protein bound	• t1/2 ~2 d		extensively metabolized	IV-Status epilepticus	*Vital and Restricted Medicine*	Additive with sedative-hypnotics	CNS and respiratory effects	Resuscitation equipment must be available

			gives peak concentration in ~1 h with 90% bioavailability		to several active metabolites	*Injection(solution for injection),Diazepam 5mg/ml,2ml ampoule* PO: *Tablets Diazepam 2mg/5mg* Per rectal *(Paeds) Rectal tubes(=rectal solution) or suppositories 2.5 mg,5mg*	*Medical Officers(L_2) and above* *Essential and Restricted Medicine Medical Officers(L_2) and above* *Vital and Restricted Medicine Medical Officers(L_2) and above*	TCAs, Carbamazepine, Phenobarbital, Phenytoin, Sodium Valproate Olanzapine,Haloperidol,Efavirenz,Ritonavir, beta-blockers,CCBs,Digoxin,grape juice etc	:Sedation, drowsiness, confusion, amnesia, vertigo, ataxia hypotension, cardiac arrest, irritability ,excitability, hallucinations, sleep disturbance, pain and thromboembolism on IV injection	

Lorazepam						IV *Injection* ,Lorazepam 4mg/ml,1 ml ampoule	*Essential Medicine Senior house Officers(L_3) and above*	Same as Diazepam	Same as Diazepam	Resuscitation equipment must be available.
Clonazepam	Absence seizures, myoclonic seizures		t1/2 20–50 h	>80% bioavailability	•extensively metabolized but no active metabolites	PO *Tablets*, Clonazepam 500 micrograms,2mg	*Essential Medicine Senior house Officers(L_3) and above*	Same as Diazepam	Drowsiness, lethargy, ataxia, paradoxical aggression, irritability, mental changes, blood disorders, abnormal liver function tests, excessive salivation	Causes drowsiness
Carbamazepine	Generalized tonic-clonic	No significan	8-12 h(• t1/2)	Well absorbed	10-11 epoxide	PO	*Essential Medicine*	Phenytoin, valproate,	Dizziness, drowsiness, headache,	Dose adjustment in renal impairment

	seizures, partial seizures	t protein binding	6-8 h(peak conc)			*Tablets(scored),*Carbamazepine 200 mg *Oral solution(syrup),*Carbamazepine 100mg/5ml,100ml bottle *Tablets* ,modified release(scored),Carbamazepine 200mg	*All interns and above(L1) and above* *Non-Essential Medicine* *All interns and above(L1) and above* *Non-Essential Medicine* *All interns and above(L1) and above*	fluoxetine, verapamil, macrolide antibiotics, isoniazid, propoxyphene, danazol, phenobarbital, primidone, etc	ataxia, blurred vision, Nausea, diplopia, ataxia, hyponatremia, headache, anorexia, abdominal pain, diarrhoea, dry mouth, constipation, cholestatic jaundice, erythematous rash, hepatitis, alopecia, SJS, arrhythmias, heart block, heart failure, depression, impotence, male	Impair performance of skilled tasks *Signs of toxicity:* Gastrointestinal disturbances eg nausea, vomiting

									gynaecomastia ,male impotence, galactorrhoea, activation of psychosis, aggression	
Lamotrigrine	Generalized tonic-clonic seizures, generalized seizures, partial seizures, absence seizures	No significant protein binding	• t1/2 25–35 h	Well absorbed	extensively metabolized, but no active metabolites	PO *Tablets, Lamotigrine 5mg,25mg,100mg*	*Essential Medicine Senior house officials and above(L_3) and above*	Valproate, carbamazepine , oxcarbazepine, phenytoin, phenobarbital, primidone, succinimides, sertraline, topiramate etc	Dizziness, headache, diplopia, Rash, serious skin reactions eg SJS,TN,,fever, malaise,leucopenia,angioedema,conjunctivitis,drowsiness, insomnia,irritability,aggression tremor, agitation, confusion	Serious skin reactions observed Whole tablets should be administered, no scoring

Sodium Valproate	Generalized tonic-clonic seizures, partial seizures, generalized seizures, absence seizures, myoclonic seizures	Highly protein bound	t1/2 9–16 h	Well absorbed from several formulations	Extensively metabolised	PO *Tablets(enteric-coated),*sodium valproate 200mg *Tablets(slow release),*sodium valproate 300mg,500mg *Oral solution (syrup),*sodium Valproate 250mg/5ml,100 bottle	*Essential Medicine Medical officers and above(L_2) and above* *Essential Medicine Medical officers and above(L_2) and above* *Essential Medicine Medical officers and above(L_2) and above*	Phenobarbital, phenytoin, carbamazepine, lamotrigine, felbamate, rifampin, ethosuximide, primidone etc	Nausea, tremor, weight gain, hair loss, teratogenic, hepatotoxic, gastrointestinal irritation, nausea, increased appetite and weight gain, oedema, hair loss, thrombocytopenia, ,rarely, hepatic failure, sedation, SJS, TEN, hearing loss, gynaecomastia	Monitor liver function Avoid sudden withdrawal

Pregabalin	Focal seizures	Not protein bound	• t1/2 4.5–7 h	Well absorbed	Not metabolised	PO *Capsules*, Pregabalin 25mg,75mg	*Non-Essential Medicine Senior house officials and above(L_3) and above*	Dizziness, Somnolence, blurred vision, diplopia, increased appetite and weight gain, dry mouth, constipation, vomiting, euphoria, irritability, ataxia	Somnolence, dizziness, ataxia	Avoid abrupt withdrawal; taper off Caution in renal impairment, severe congestive heart failure and pregnancy
Gabapentin	Generalized tonic-clonic seizures, partial seizures, generalized seizures	Not protein bound	• t1/2 5–8 h	Bioavailability 50%, decreasing with increasing dose	Not metabolized	PO *Capsules*, Gabapentin 100mg,300mg	*Non-Essential Medicine Senior house officials and above(L_3) and above*	Morphine, Antacids, Mefloquine, TCAs, MAOIs, Antipsychotics	Somnolence, dizziness, ataxia, drowsiness, diplopia, tremor, weight gain, pharyngitis, amnesia, headache	Caution in renal impairment Monitor for hypersensitivity

Topimarate	Generalized tonic-clonic seizures, partial seizures, generalized seizures, absence seizures, migraine	No protein binding	• t1/2 20 h, but decreases with concomitant drugs	Well absorbed	No active metabolites 40% excreted in urine	PO *Tablets*, film coated, Topimarate 25mg,100mg	*Non-Essential Medicine Senior house officials and above(L_3) and above*	Phenytoin, carbamazepine, oral contraceptives, Lamotrigine, lithium	Somnolence, cognitive slowing, confusion, paraesthesia, abdominal pain, dry mouth depression, metabolic acidosis, thrombocytopenia, serious skin reactions	Monitor for visual disturbances and intra-ocular pressure

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30th June 2020

KENYATTA NATIONAL HOSPITAL APPROVED 30 JUN 2020 KNH/UoN-ERC P. O. BOX 20723 - 00202 NAIROBI

Faith Mwende Munyasya
Reg. No. U51/11269/2018
Dept. of Pharmacology and Pharmacognosy
School of Pharmacy
College of Health Sciences
University of Nairobi

Dear Faith,

RESEARCH PROPOSAL – CLINICAL AUDIT OF ACUTE SEIZURE MANAGEMENT IN PAEDIATRIC PATIENTS AT KENYATTA NATIONAL HOSPITAL (P981/12/2019)

This is to inform you that the KNH- UoN Ethics & Research Committee (KNH- UoN ERC) has reviewed and **approved** your above research proposal. The approval period is 30th June 2020 – 29th June 2021.

This approval is subject to compliance with the following requirements:

a. Only approved documents (informed consents, study instruments, advertising materials etc) will be used.
b. All changes (amendments, deviations, violations etc.) are submitted for review and approval by KNH-UoN ERC before implementation.
c. Death and life threatening problems and serious adverse events (SAEs) or unexpected adverse events whether related or unrelated to the study must be reported to the KNH-UoN ERC within 72 hours of notification.
d. Any changes, anticipated or otherwise that may increase the risks or affect safety or welfare of study participants and others or affect the integrity of the research must be reported to KNH- UoN ERC within 72 hours.
e. Clearance for export of biological specimens must be obtained from KNH- UoN ERC for each batch of shipment.
f. Submission of a request for renewal of approval at least 60 days prior to expiry of the approval period. (*Attach a comprehensive progress report to support the renewal*).
g. Submission of an *executive summary* report within 90 days upon completion of the study. This information will form part of the data base that will be consulted in future when processing related research studies so as to minimize chances of study duplication and/ or plagiarism.

For more details consult the KNH- UoN ERC website**http://www.erc.uonbi.ac.ke**

Yours sincerely,

PROF. M. L. CHINDIA
SECRETARY, KNH-UoN ERC

c.c. The Principal, College of Health Sciences, UoN
The Director, CS, KNH
The Chairperson, KNH- UoN ERC
The Assistant Director, Health Information, KNH
The Dean, School of Pharmacy, UoN
The Chair, Dept. of Pharmacology and Pharmacognosy, UoN
Supervisors: Dr. Eric M. Guantai, Dept. of Pharmacology and Pharmacognosy, UoN
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Study Registration Certificate

1. Name of the Principal Investigator/Researcher
   DR. FAITH MWENDE MUNYASYA
2. Email address: faithymwende6@gmail.com Tel No. 0715417876
3. Contact person (if different from PI).....
4. Email address: ..... Tel No. .....
5. Study Title
   CLINICAL AUDIT OF ACUTE SEIZURE MANAGEMENT IN PAEDIATRIC PATIENTS AT KENYATTA NATIONAL HOSPITAL
6. Department where the study will be conducted PAEDIATRICS
   (Please attach copy of Abstract)
7. Endorsed by Research Coordinator of the KNH Department where the study will be conducted.
   Name: ..... Signature ..... Date .....
8. Endorsed by KNH Head of Department where study will be conducted.
   Name: Makewa dr Signature ..... Date 27/07/20
9. KNH UoN Ethics Research Committee approved study number P981/12/2019
   (Please attach copy of ERC approval)
10. I DR. FAITH MWENDE MUNYASYA commit to submit a report of my study findings to the Department where the study will be conducted and to the Department of Research and Programs.
    Signature ..... Date 27/07/2020
11. Study Registration number (Dept/Number/Year) Paed/NATIONAL/232/2020
    (To be completed by Research and Programs Department)
12. Research and Program Stamp

KENYATTA NATIONAL HOSPITAL * Research Resource Centre * P.O. Box 20723-00202 Nairobi
12 AUG 2020

All studies conducted at Kenyatta National Hospital **must** be registered with the Department of Research and Programs and investigators **must commit** to share results with the hospital.