PREVALENCE OF INTRACTABLE EPILEPSY AND ASSOCIATED FACTORS AMONG CHILDREN WITH EPILEPSIES ATTENDING PEDIATRIC NEUROLOGY CLINIC AT MUHIMBILI NATIONAL HOSPITAL, DAR ES SALAAM, TANZANIA

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By

Obrey Harold Urio

A Dissertation Submitted in (Partial) Fulfilment of the Requirements for the Degree of Master of Medicine (Paediatrics and Child Health) of

Muhimbili University of Health and Allied Sciences
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CERTIFICATION.

The undersigned certify that they have read and hereby recommend for acceptance by Muhimbili University of Health and Allied Sciences a dissertation titled '***Prevalence of intractable epilepsy and associated factors among children with epilepsies attending pediatric neurology clinic at Muhimbili National Hospital, Dar es salaam Tanzania'***, (partial) fulfilment of the requirements for the degree of Master of Medicine (Paediatrics and Child Health) of the Muhimbili University of Health and Allied Sciences.

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DECLARATION AND COPYRIGHT

I, Obrey Harold Urio, I declare that this **dissertation** is my original work and it has not been presented and shall not be presented to any other University for a similar or any other degree award.

Signature..... **Date…….....**

AKNOWLEDGMENT

I thank God for family, health and above all the gift of life.

I am thankful to my supervisors Dr Helga Naburi, Dr Edward Kija and Dr Hilda Makungu for their guidance and encouragement throughout this work.

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In a special way I want to thank my dear beautiful Wife Dr Lydia Mamseri Urio, my beautiful daughter Brigett Urio, and my wonderful mother Heavenlight Urio for their support, encouragement and motivation.

In Loving Memory of My Father, Harold E Urio , "*We will hold you in our hearts until we see you in Heaven".*

DEDICATION

This work is dedicated to sick children at Muhimbili National Hospital.

ABSTRACT

Background: Epilepsy is one of the most common neurological disorders of childhood. Eighty percent of patients with epilepsy dwell in developing countries with majority (90%) of patients in Sub Sahara Africa (SSA) being younger than 20 years. A quarter of all children with epilepsy will be intractable to medical treatment with higher risk of morbidity and mortality despite state of the art medical management.

Locally, there is paucity of data on the magnitude of intractable epilepsy and therefore, this study aimed to establish pediatric specific prevalence of intractable epilepsy and associated factors among children with epilepsies in Tanzania.

Objectives: To determine the prevalence of intractable epilepsy and associated factors among patients with epilepsies aged between 3 months to 15 years attending pediatric neurology clinic at Muhimbili National Hospital, Dar es Salaam Tanzania.

Method: This was hospital based cross sectional study, which was conducted among children with epilepsies attending pediatric neurology outpatient clinic at Muhimbili National Hospital Dar es Salaam Tanzania. Structured questionnaire was used to collect demographic and clinical information. Seizures and epilepsies were classified using 2017 International League Against Epilepsy (ILAE) classification.

Descriptive analysis was summarized using proportions and median with interquartile ranges (IQR). Overall prevalence of intractable epilepsy was calculated with 95% confidence interval. Chi squire and where applicable Fischer's exact test was used to determine association between categorical variables.

Logistic regression was used to determine independent factors associated with intractable epilepsy. Probability value (p) value of < 0.05 was considered statistically significant.

Results: A total of 236 children who fulfill the diagnostic criteria of epilepsy and who were on treatment with Anti Epileptic Drugs (AED) for more than 3 months were consecutively

recruited in this study. Median age of the participants was 72 months (IQR=42-78). There was slight male preponderance by 56%. Prevalence of intractable epilepsy was found to be 14.8%, 95% CI (10.6-20%). Out of 35 patients with intractable epilepsy, 60% had generalized epilepsy and almost a quarter had a diagnosis of epilepsy syndrome, the commonest being Lennox Gastaut Syndrome (LGS). Eighty percent of all patients with IE had structural lesions which were visualized on MRI, the commonest being cystic encephalomalacia observed in 34% of patients. At least half (54.4%) of patients with focal intractable epilepsy had lesions that could be amenable to curative epilepsy surgeries.

Independent factors associated with intractable epilepsy were; onset of seizures during the first months of life (OR =3.5; 95% CI 1.2-10; P= 0.02) and high initial seizures frequency (OR=4.2; 95% CI 1.8-9.6; P=<0.001).

Conclusion and recommendations: Almost 15% of all patients with epilepsy attending pediatric neurology clinic were found to have (IE). Independent predictors for Intractable Epilepsy were neonatal onset seizures and high initial seizures frequency. Patients with IE were more likely to present with generalized epilepsies and about a quarter were diagnosed with epilepsy syndromes. More than three quarters of patients with IE had structural abnormality noted on MRI

Patients with neonatal onset seizures and high seizures frequency should be followed up closely, for early diagnosis of intractable epilepsy. Intervention research is recommended in this study setting to assess the utility of ketogenic diet and epilepsy surgery for those with epilepsy syndromes and structural brain lesions that can be modified by epilepsy surgery.

MUHTASARI

Utambulisho: Kifafa ni miongoni mwa ugonjwa unaaongoza kati ya magonjwa yanayohusisha mfumo wa neva kwa watoto. Asilimia 80 ya watu wote wenye ugonjwa wa kifafa wanaishi katika nchi zinazoendelea ,miongoni mwao asilimia 90 wanaoishi katika mataifa yanayopatikana kusini mwa jangwa la Sahara na wana umri chini ya miaka ishirini.
Robo ya watoto wote wanaopata ugonjwa wa kifafa ,wanakua sugu kwa dawa hata endapo watatumia dawa mpya za kisasa zaidi, na wagonjwa hawa wanakua kwenye hatari kubwa ya kupata matatizo ya kiafya na kupoteza maisha mapema.
Kutokana na uhaba wa taarifa kuhusu ukubwa wa tatizo la kifafa sugu, tafiti hii iliandaliwa ili kuweza kutambua ukubwa wa tatizo hili kwa watoto na visababshi vyake miongoni mwa watoto wenye kifafa.

Malengo: Kutambua ukubwa wa tatizo la kifafa sugu na visababishi vyake miongoni mwao watoto wenye kifafa walio na umri kati ya miezi mitatu mpaka miaka kumi na mitano wanaohudhuria kliniki ya watoto wenye matatizo ya mfumo wa neva katika hosipitali ya taifa Muhimbili.

Njia: Utafititi huu ulifanyika katika hosipitali ya taifa Muhimbili kwa kuzingatia njia za kisayansi za utafiti. Dodoso lilitumika kukusanya taarifa za kidemografia na taarifa za matibabu .Ugonjwa wa kifafa na degedege uligawanywa kwenye makundi kwa kutimia makubaliano ya kimataifa ya ugawanywaji wa degedege na kifafa (ILAE 2017).

Majibu: Jumla ya watoto 236 waliokua na kifafa na waliokua tayari wamekwisha kutumia dawa kwa kipindi cha angalau miezi mitatu walijumuishwa katika tafiti hii.Umri wa wastani wa watoto walioshiriki ilikua ni miezi 72. Wavulana walikua wengi kuliko wasichana kwa wastani wa asilimia 56.

Asilimia 14.8 ya watoto wote wenye kifafa waligundulika kua na kifafa kisichosikia dawa (kifafa sugu).

Kati ya watoto 35 waliokua na tatizo la kifafa sugu,asilimia sitini walikua na degedege la pande zote za mwili na robo ya watoto hawa walikua na sindromu za degedege na iliyoongoza ni ile inayoitwa Lennox Gaustat Syndrome.

Asilimia 80 ya watoto wenye kifafa sugu walipatikana kua na matatizo kwenye maumbile ya ubongo wao walipofanyiwa kipimo cha MRI ,na tatizo la kimaumbile liitwalo cystic encephalomalacia liliongoza kwa ukubwa. Karibu nusu ya wagonjwa wote wenye kifafa sugu kinachoambatana na degedege za upande mmoja walionekana kuwa na makovu kwenye ubongo ,ambayo yanaweza kutibika kwa njia za upasuaji wa kutibu degedege.

Visababishi vya kifafa sugu vilivyogundulika ni pamoja na kuanza kupata degedege ndani ya kipindi cha mwezi mmoja wa kuzaliwa(OR=3.9;95% CI 1.2-10;P=0.02) na kupata degedege mara nyingi mfululizo kabla ya kuanza matibabu (OR =4.2;95% CI 1.8-9.6);P<0.001.)

Muhtasari na Mapendekezo: Karibu asilimia 15% ya watoto wote wenye kifafa wanaohudhuria kliniki ya magonjwa ya neva katika hosipitali ya taifa Muhimbili walikua na kifafa sugu. Visababishi vya kifafa sugu vilivyogundulika ni pamoja na kuanza kupata degedege ndani ya mwezi mmoja wa kuzaliwa na kupata degedege mara nyingi kabla ya kuanza matibabu. Wengi wa wagonjwa waliokua na kifafa sugu walikua wakipata degedege za pande zote mbili za mwili huku robo yao wakiwa na syndromu za kifafa. Zaidi ya robo tatu ya wagonjwa waliokua na kifafa sugu pia walikua na matatizo ya kimaumbile katika ubongo wao.

Tunapendekeza watoto wanaopata degedege katika kipindi cha mwezi mmoja wa kuzaliwa na wanaopata degedege mara nyingi mfululizo wafuatiliwe kwa ukaribu zaidi ili kujua kama kifafa chao ni sugu.

Pia tunapendekeza ifanyike tafiti ya kuangalia ufanisi wa upasuaji pamoja na njia nyingine katika kutibu kifafa sugu.

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ABBREVIATIONS

AED	Anti Epileptic Drugs
CT	Computed Tomography
EEG	Electroencephalogram
IE	Intractable Epilepsy
ILAE	International League Against Epilepsy
IRB	Institutional Review Board
LMIC	Low and Middle Income Countries
MNH	Muhimbili National Hospital
MRI	Magnetic Resonance Imaging
MUHAS	Muhimbili University of Health and Allied Sciences
SD	Standard Deviation
SPSS	Statistical Package For Social Sciences
SSA	Sub Saharan Africa
USA	United States of America

DEFINITIONS OF TERMS

Epilepsy is defined as at least two unprovoked (or reflex) seizures occurring >24 h apart, or unprovoked (or reflex) seizure and a probability of further seizures similar to the general recurrence risk (at least 60%) after two unprovoked seizures or occurring over the next 10 years, or diagnosis of an epilepsy syndrome (1).

Intractable epilepsy is defined as failure of adequate trials of two tolerated and appropriately chosen and used anti epileptic drug schedules (whether as monotherapy or in combination) to achieve sustained seizure control (2).

Sustained seizure control is defined as seizure free period for at least one year since initiation or change of Anti Epileptic Drugs (2).

Focal seizures-originates from an area or network of cells on one side of the brain (1).

Generalized seizures-originates from networks on both sides of the brain at the onset (1).

Unknown onset-If the onset of a seizure is not known. Later on, the seizure type can be changed if the beginning of a person's seizures becomes clear (1).

Focal to bilateral seizure-A seizure that starts in one side or part of the brain and spreads to both sides (1).

Focal motor seizure-This means that some type of movement occurs during the event (1).

Focal non-motor seizure: This type of seizure has other symptoms that occur first, such as changes in sensation, emotions, thinking, or experiences (1).

Retained awareness- means that the person was aware of self and environment during the seizure, even if immobile (1).

Tonic- A sustained increase in muscle contraction lasting a few seconds to minutes (1).

Tonic–clonic- A sequence consisting of a tonic followed by a clonic phase (1).

Myoclonic- Sudden, brief (<100 msec) involuntary single or multiple contraction(s) of muscles(s) or muscle groups of variable topography (axial, proximal limb, distal) (1).

Myoclonic–atonic -A generalized seizure type with a myoclonic jerk leading to an atonic motor component (1).

Automatism- A more or less coordinated motor activity usually occurring when cognition is impaired and for which the subject is usually (but not always) amnesic afterward (1).

Emotional seizures- Seizures presenting with an emotion or the appearance of having an emotion as an early prominent feature, such as fear, spontaneous joy or euphoria, laughing (gelastic), or crying (dacrystic) (1).

Epileptic spasms- A sudden flexion, extension, or mixed extension–flexion of predominantly proximal and truncal muscles that is more sustained than a myoclonic movement but not as sustained as a tonic seizure. Other Limited forms to be considered include grimacing, head nodding, or subtle eye movements (1).

1.0 INTRODUCTION

1.1 Background.

Epilepsy is a disease of the brain defined by any of the following conditions, at least two unprovoked (or reflex) seizures occurring >24 hours apart or one unprovoked (or reflex) seizure and a probability of further seizures similar to the general recurrence risk (at least 60%) after two unprovoked seizures or occurring over the next 10 years and diagnosis of an epilepsy syndrome (3). Despite good outcome with treatment, more than a quarter of epileptic patients are intractable to medical management (2).

Intractable epilepsy is defined as failure of adequate trials of two tolerated and appropriately chosen and used anti epileptic drug schedules (whether as monotherapy or in combination) to achieve sustained seizure control (2).

1.1.1 Magnitude of Epilepsy

Epilepsy is one of the commonest neurological disorders of childhood with up to 50 million people affected worldwide. Seventy five percent of people with epilepsy live in developing countries (4). Each year 3.5 million new cases are reported of which 40% occur in children under the age of 18 years and more than 80% live in developed countries (4,5). During treatment with variety of Antiepileptic Drugs (AED) up to 19 -30% of these children continue to have debilitating seizures (6,7). These patients suffer psychological problems, stigmatization, reduced quality of life and are at increased risk of mortality (8).

1.1.2 Classification of Seizures and Epilepsies

Because of the potential therapeutic implication, it is imperative to classify patients during the initial presentation into seizure and epilepsy type(s) and identify possible etiology. (**Appendix 02**) (9). Lack of diagnostic uniformity due to challenges in using standardized criteria leads to difficulties in comparing findings from different epilepsy studies especially in Low and Middle Income Countries (LMIC) (10,11).

1.1.3 Clinical Presentation

Despite the challenges of identifying intractable epilepsies from the initial presentation, it is known that, patients with refractory epilepsy are likely to present with multiple seizures types during initial presentation, high seizures frequency, neonatal onset seizures, neurological impairment and will fail to respond to initial AEDs (12–14).

1.1.4 Investigations

Electroencephalogram (EEG) is an important ancillary test since it can help to distinguish generalized from focal onset seizures, support an epilepsy diagnosis and localize the foci of focal seizures (15). Despite being used to predict the risk of intractability and its limitations, both invasive and non-invasive EEG play a pivotal role in pre surgical evaluation of patients for epilepsy surgeries (12,16).

Magnetic Resonance Imaging (MRI) is the imaging investigation of choice in epilepsy because of its better resolution in differentiating grey and white matter and abnormal and normal tissue. In patients with refractory focal seizures, MRI identifies structural abnormality, define its extent and any relationship to eloquent structures and hence it’s utility in pre surgical evaluation. The most likely underlying structural abnormalities in focal refractory epilepsy are hippocampal sclerosis, cortical scarring and congenital malformations of cortical development (17).

1.1.5 Treatment

Management of patients with intractable epilepsy is challenging because the underlying mechanisms of intractability are not completely understood. The proposed pathogenesis underlying intractable epilepsy are likely to be multifactorial with both genetic and environmental components (18). Several hypotheses have been postulated including (18),

- Over expression of multidrug efflux genes.
- Epilepsy-induced alteration of cellular targets of AED leading to a reduction in sensitivity.
- Seizures-induced formation of an abnormal neural network.
- Inherent resistance that is governed by genetic variants of proteins that are involved in the pharmacokinetics and pharmacodynamics of AED activity.
- Drug intractability due to increased disease severity.

After failure of two AED, the chance of inducing remission with sequential addition of another drug is minimal, hence drugs with different mechanisms of action should be considered for synergistic effect (19). Different surgical modalities, ketogenic diet, vagus nerve and trigeminal nerve stimulation are alternative modalities, which have been found to induce remission or significant reduction in seizures frequency (20,21). Majority of common childhood epilepsy syndromes despite being intractable to medical management, have been found to respond exceptionally well to ketogenic diet which is recommended as first line treatment for certain epilepsies (22). Patients with IE associated with structural lesions can benefit from surgical intervention, but also various palliative surgeries including the use of implantable device which can significantly improve the quality of life (23).

Understanding magnitude of intractable epilepsy in our setting is important especially taking into consideration the availability of alternative modalities of treatment.

1.2 Problem statement.

Epilepsy is one of the most common neurological disorders of childhood. It is estimated that developing countries contribute 80% of the global burden of epilepsy (4) with 90% of all patients with epilepsy in SSA being younger than 20 years (5).In Tanzania the prevalence of epilepsy among children is estimated to be 2.91 per 1,000 children (24).

Due to pervasive effects of recurrent seizures, lifelong seizures freedom is the ideal outcome of treatment. Unfortunately up to a quarter of all children with epilepsy are intractable to medical management despite timely and good choice of AED.

It is also known that, age of onset of seizures, high seizure frequency, multiple seizure types, imaging abnormalities and diagnosis of some epilepsy syndrome are factors associated with medical intractability (12,13).

Alternative treatment modalities including curative surgeries in IE associated with structural lesions and ketogenic diet have been shown to improve quality of life and decrease morbidity associated with recurrent seizures (22,23).

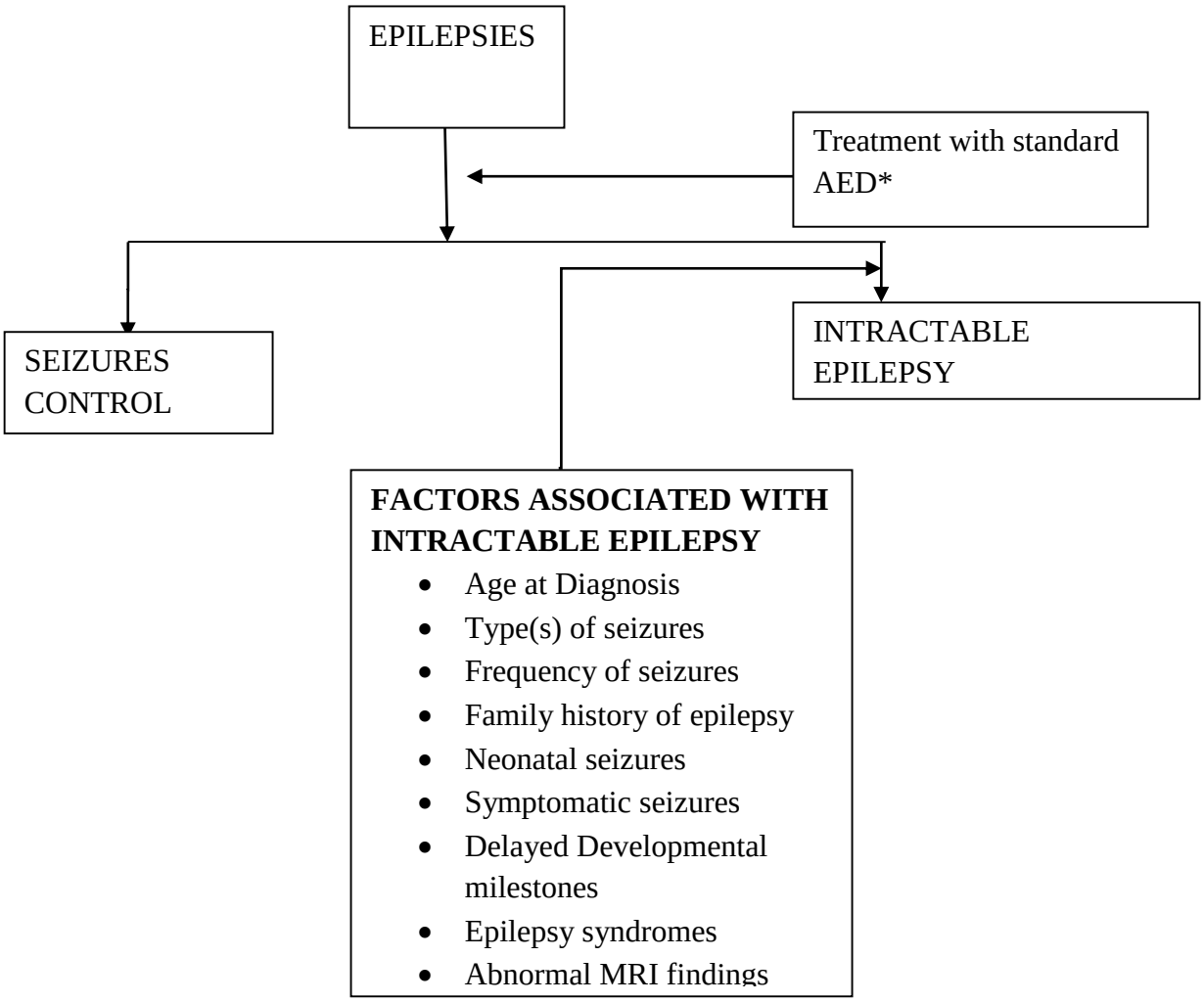
In Tanzania despite epilepsy being one of the common causes of morbidity there are no studies conducted on intractable epilepsy among children despite its known effect both on neurodevelopment and overall quality of life. Furthermore, potential risk factors for developing intractable epilepsy are many and occur during childhood, hence the need to carry out this study. Results from this study will provide baseline data on the prevalence of intractable epilepsy and associated factors so that early prediction of intractability and early choice of alternative therapies including ketogenic diet and or epilepsy surgery where indicated can be made.

1.3 Rationale

Most of patients with epilepsy (90%) in SSA are young people less than 20 years of age, and almost one in every four children with epilepsies is resistant to standard anti-epileptic drugs despite timely and proper choice of drugs. Alternative treatment modalities such as, epilepsy surgery, Vagus Nerve Stimulation (VNS) and ketogenic diet have been shown to improve quality of life among patients with IE. Thus understanding the magnitude and predictors of intractable seizures is a key step towards early diagnosis and deciding the next step of management. This study aims to determine the prevalence and identify the factors associated with intractable epilepsy among children with epilepsies attending pediatric neurology clinic at Muhimbili National Hospital (MNH) Tanzania. The findings from this study will provide pediatric specific prevalence of intractable epilepsy in Tanzania. Findings will also help to create a simple guide for early prediction of intractable epilepsy, which will assist in understanding prognosis and potential alternative treatment options.

1.4 Conceptual framework

Conceptual framework for intractable epilepsy and associated factors**.**



Standard AED* Anti epileptic drugs specific for seizure type, applied for adequate duration and dosage.

Figure 1: Conceptual framework description

After treatment with standard AEDs patients will have complete remission of seizures or become intractable to AEDs. The intermediate modifiers of treatment response are the factors known to be associated with IE. Among these are, focal epilepsies, high seizure frequency and symptomatic seizures (25).Others are ,delayed developmental milestones, epilepsy syndromes, structural brain abnormalities seen on MRI and specific EEG findings (25,26).

1.5 Research questions

1) What is the prevalence of intractable epilepsy among patients with epilepsies on AEDs aged between 3 months and 15 years attending pediatric neurology clinic at MNH?
2) What are the clinical types of seizures among children aged 3 months to 15 years with intractable epilepsy attending pediatric neurology clinic at MNH?
3) What are the EEG and neuro imaging findings among patients aged 3 months to 15 years with intractable epilepsy attending pediatric neurology clinic at MNH?
4) What are the factors associated with intractable epilepsy among children with epilepsies attending pediatric neurology clinic at MNH?

1.6 Objectives

1.6.1Broad objective

To determine the prevalence of intractable epilepsy, clinical patterns of epileptic seizures and associated factors among children with epilepsy aged between 3 months to 15 years attending pediatric neurology clinic at MNH.

1.6.2 Specific objectives

1. To determine the prevalence of intractable epilepsy among patients with epilepsies on anti epileptic drugs aged between 3 months to 15 years attending pediatric neurology clinic at MNH.
2. To determine clinical patterns of epileptic seizures among patients with intractable epilepsy aged between 3 months to 15 years attending pediatric neurology clinic at MNH.
3. To determine factors associated with intractable epilepsy among patients with epilepsy aged between 3 months to 15 years attending pediatric neurology clinic at MNH.

2.0 LITERATURE REVIEW

2.1 Magnitude of intractable epilepsy

The magnitude of intractable epilepsy among children have been studied well in prospective studies in developed countries while not much is known in LMIC, despite contributing more than three quarters of the world epilepsy burden. There are inconsistencies in the magnitude of intractable epilepsy between different studies which are mainly attributed to various factors including differences in case definition used (27).

Studies have shown the prevalence of intractable epilepsy in children to range between 20-30% (7). For example, in a prospective study done in Scotland among patients who had their first seizure before the age of 16 years and followed for 37 years, 19% were found to be resistant to AEDs (6). Similarly, in Unites States 23.2% of all children with epilepsy were found have intractable epilepsy (19). In Nigeria17.2% of children diagnosed with epilepsy were found to be intractable to medical management during their follow up (28).

2.2 Factors associated with intractable epilepsy

Previous studies have found a consistent association between young age at onset of seizures and risk of developing medical intractability (14,29,30). Wirell et al in USA found that, diagnosis of epilepsy before one year of age was strongly associated with risk of refractoriness to AED, whereas up to two thirds of cases of intractable epilepsy are diagnosed within the first year of life (26).

Kwan et al in Scotland found high initial seizures frequency at onset to be strongly associated with intractable epilepsy (19). This association has been found to be the case in studies done in other centers (14,26). Repeated seizures have been shown to cause neuronal loss and other structural and functional changes which lead to formation of excitatory recurrent circuits (31).

Epilepsy types and some seizure types have been shown to be associated with intractable epilepsy. For instance, studies from developed countries have found focal epilepsy to be associated with high risk of intractability compared to generalized epilepsy (29,32).

Chawla et al demonstrated a strong association between intractable epilepsy and myoclonic seizures while other motor and non motor forms of generalized epilepsies have been found to have good prognosis (13). Additionally having more than one seizure type at presentation is known to be associated with intractability (32).

Other important predictor of intractable epilepsy is a history of neonatal seizures (13,14). Seizures in the immature brain result in non pruning of neurons, increase number of gap junctions and abnormal connectivity which predisposes the brain to low seizures threshold (33).

Epilepsy syndromes have been found to be an important predictor of epilepsy outcome with some being resistant to medical management. West syndrome which is one of childhood epilepsy syndrome have been associated with high risk of medical intractability in studies done from different centers (34,35).

Furthermore, Jeong et al observed that, among patients with tuberous sclerosis, those presenting with infantile spasms were more likely to be refractory to medical treatment (36). Other typical refractory generalized epilepsy in children are, Ohtahara syndrome, early myoclonic encephalopathy, Lennox-Gaustat syndrome (LGS) and Dravet syndrome (37).

Abnormal neurological examinations and delayed developmental milestones are amongst other factors known to be associated with intractable epilepsy (35). Wirrell et al found a strong association between developmental delay at the initial diagnosis of epilepsy and intractability (26).Similarly, abnormal neurological examination and microcephaly have been found to be associated with IE (12,13).

Presence of structural brain abnormality increase the risk of poor response to AED (29). Structural and functional changes of central nervous system (CNS) lead to hyper-excitability, abnormal capillary endothelial cells of blood-brain barrier and over-expression of efflux transporters and ultimately medical intractability (38).

Twin studies have postulated that genes and, therefore, family history may be relevant to the pathogenesis of epilepsy but less so to the treatment outcome (39). For first degree relatives the risk of recurrence of epilepsy is known to be 5-10 fold compared to general population (40), with the risk being an interplay of genetic and environmental factors that lowers an individuals seizure threshold (41).

In Scotland, Hitiris et al found association between family history of epilepsy and later risk of intractability in adulthood (42). Among patients with Dravet syndrome which is one of the epilepsy syndromes, 10% of their parents were found to be mosaic carriers of genetic mutations associated with the condition. Few mutations also inherited from asymptomatic parents have been found to be associated with chanelopathies associated with intractable epileptic syndromes (43).

EEG is an important tool both in evaluation and prediction of IE (12). A study done by Ko et al demonstrated abnormalities such as slowing and asymmetries of the background to be strongly associated with intractable epilepsy (29).

Similarly, Wirell et al demonstrated association between focal slowing on EEG and risk of intractability (26). Furthermore, focal and multifocal epileptic form discharges and burst suppression pattern are more common in intractable epilepsy (12).

Some neuro-radiological abnormalities have been found in different studies to be associated with the risk of medical intractability (12,36). Representative of these common findings are, hippocampal sclerosis, amygdaloid sclerosis, coarse and macroscopic brain malformation (focal cortical dysplasia, hemimegalencephaly, tuberous sclerosis), and destructive lesions (44).

3.0 MATERIAL AND METHODS

3.1 Study Design

This was a hospital based cross-sectional study.

3.2 Study Area

This study was conducted at Muhimbili National Hospital (MNH) in Dar es Salaam, the largest business city in Tanzania. MNH is the national referral and university teaching hospital with approximately 1500 bed capacity and cater for up to 1200 outpatient per day and more than 1000 admissions per week.

The hospital has a pediatric building, which contains 8 pediatric wards (for pediatric patients with various medical and surgical conditions), pediatric operating theaters, pharmacies, and pediatric Intensive Care Unit (PICU). Hospital costs including investigations, medications and consultations are either covered by insurance schemes, out of pocket or a special waver for some or all services for patients with financial constraints.

MNH has a capacity to do investigations such as MRI, Computed Tomography (CT) scans, EEG and an array of blood investigations. Results of all investigations are posted in to the hospital database (Jeeva^{TM}). The respective doctors with access code can access the database containing results and other patient information for both in patients and outpatients.

Pediatric neurology clinic at MNH receives complex neurological cases referred from all over the country. The clinic is located in the Pediatrics Complex where two pediatric neurologists, general pediatricians, paediatric residents and medical officers from pediatric neurology ward are responsible for patients care. The clinic is conducted twice a week, Monday and Wednesday from 09:00 Am to 5:00 Pm. After registration, vital signs and weight is taken before patients are directed to the consultation rooms. The clinical information obtained by the attending physician is entered in the hospital electronic database (Jeeva^{TM}) and medications are prescribed and dispensed online.

The clinic serves about one hundred patients (majority having neurological conditions) per week. A pilot study conducted prior found that, at lest 50-60% of all patients seen in the clinic per week have seizure disorders.

Neurologists or pediatricians prescribe AEDs of which the choice is based on the type of epilepsy. Dosages are calculated based on the body weight and patients are initially given two weeks of follow up and thereafter their medications are sequentially titrated against seizures frequency as reported by the care taker. Medications are reviewed and doses are adjusted if needed. Based on seizures control the follow up interval is progressively increased up to three monthly for patients with adequate seizures control.

Commonly prescribed old generation and some new generation AED are available at MNH paediatric pharmacy and are dispensed by pharmacists in different formulations depending on child age and tolerance. Where necessary, some of the new generation AED that are not available at MNH are prescribed and patients are requested to purchase from private pharmacies.

3.3 Study Duration

This study was conducted for a period of 12 months from June 2020 to June 2021.

3.4 Study Population

All children with epilepsy aged between 3 months to 15 years attending pediatric neurology clinic at Muhimbili National Hospital.

Inclusion Criteria

- All patients between the age of three months to fifteen years attending pediatric neurology clinic who fulfill the diagnostic criteria of epilepsy and who have been on anti epileptic drugs for at least three months.
- 3 months of treatment were required for a clinically significant therapeutic effect of AED, hence the minimum age at recruitment to this study.
- Paediatric unit at MNH attend to children up to the age of 15 years hence the maximum age of recruitment.

Exclusion Criteria

- All patients between the ages of three months to 15 years with epilepsies whose caregivers did not give consent.

3.5 Sample Size Calculation

Sample size was calculated using Kish Leslie formula using a proportion of 17.2%, the proportion of intractable epilepsy among children with epilepsy in Nigeria, a study done by Lagunju et al in 2011 (28).

$$N=\frac{Z^2p\,(1-p)}{\varepsilon^2}$$

$$\frac{1.96^2 \times 0.172\,(1-0.172)}{0.05^2} = 219$$

Where,

Z=Level of confidence

P=Expected proportion

Ɛ=Margin of error

With assumption of margin of error of 5% at 95% confidence level and 5% non-response rate, the minimum sample size was 230.

3.6 Sampling Procedure

Patients who met the eligibility criteria were consecutively recruited into this study until desired sample size was reached

3.7. Variables

3.7.1 Dependent variable

Intractable epilepsy (failure to achieve seizure freedom after adequate trial of two appropriately chosen and used anti epileptic drugs)

3.7.2 Independent variables

Demographic parameters: Age of the patient, sex, and age at onset of seizures, occupation of the caregiver.

Clinical parameters: seizure types, estimated number of seizures per day, family history of epilepsy. Developmental delay, fever at or preceding seizures onset, delayed crying at birth, history of resuscitation, history of head trauma preceding seizures, history of status epilepticus (defined as history of having seizures for more than 30 minutes, or having two episodes of seizures without regaining consciousness in between the two episodes) at any point since diagnosis.

Medications: Types, dose, duration of use and history of optimization of anti epileptic drug used (to see if the trial of medications was appropriate and adequately applied) and self-reported adherence.

3.8 Data Measurement

3.8.1 Outcomes measurement.

All patients who did not achieve remission after adequate trial of appropriately chosen anti epileptic drugs were regarded as having intractable epilepsy.

Any documented attempt to titrate the dose up over the past three months defined adequate trial of Anti Epileptic Drugs.

Appropriate chosen anti epileptic drugs meant the choice was appropriate for the epilepsy type.

Seizure freedom meant freedom from any seizures for more than three times the pre intervention inter-seizure interval prior to initiation of treatment.

Brain MRI was the only imaging modality included in this analysis. Findings were dichotomized into normal or abnormal, followed by the radiological diagnosis.

EEG reports were recorded as normal or abnormal followed by type of epileptiform discharges noted.

3.9 Data collection tools and procedure.

Data was collected using a researcher administered, pre tested standardized structured questionnaire. The researcher developed the questionnaire based on available literature on the topic, however classification of seizures and epilepsy was adopted from 2017 ILAE recommendations **(Appendix 1 and 2)**. The questionnaire was translated to Kiswahili and back translated by a different person before it was used for a pilot study.

Research assistant, a medical officer working with the neurology unit who is a certified Pediatric Epilepsy Trainee (PET) by British Pediatric Neurology Association (BPNA), and the principal investigator administered the questionnaire.

Demographic and clinical information was obtained by interviewing the caregiver and information was entered in the questionnaire.

MRI and EEG reports were obtained from the hospital electronic database or printed reports given by the caregivers.

Current chronological and developmental age was assessed and compared using a simple guide attached in the questionnaire **(Appendix 3).** AED dose was calculated per body weight and any attempt to titrate the dose, change, or add another medication and duration since the change as stated by the care taker and verified from the patient previous visits was recorded.

3.10 Data management and analysis

Data entry and cleaning was done using statistical package for social science (SPSS V25) Inc. Chicago, IL.

Measures of central tendency were used to summarize continuous data. Charts and tables were used to display categorical data.

Proportion of patients with intractable epilepsy was calculated from all patients with epilepsy attending pediatric neurology outpatient clinic during the study period. Contingency tables were constructed for bivariate analysis to explore the factors associated with intractable epilepsy. Chi squire test and Fisher's exact test where applicable were used to determine the association between dependent and independent variables. The level of significance was set at $p<0.05$.

Univariate and multivariate logistic regression models were used to determine the odds ratios and p values for factors associated with intractable epilepsy. Only those factors whose Odd ratios had p values <0.2 on univariate were included in multivariate analysis model, using forward selection method. Results are reported as adjusted odds ratio, 95%CI and p values for each variable included in the final model. For all analysis $p<0.05$ was considered statistically significant.

3.11 Ethical Consideration

Ethical approval was obtained from the MUHAS Directorate of research and publication,

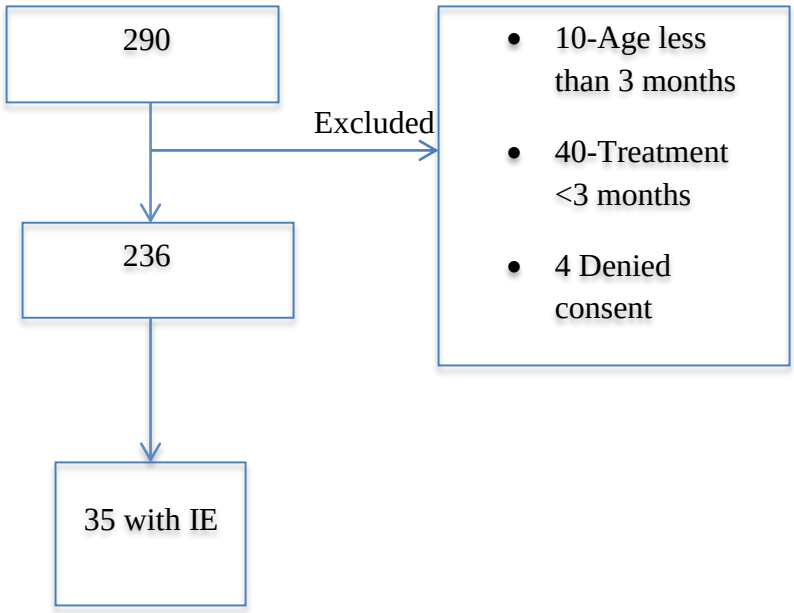
Institution Review Board (IRB #: MUHAS-REC-04-2020-266). Permission to conduct this study was obtained from Directorate of Research, Training and Consultancy at MNH. Caregivers were informed about the study including the importance of doing it and the procedures involved and after they understood and accepted to participate, they were requested to sign a written consent before enrollment. Strict confidentiality was maintained by use of a study identification number assigned to each participant. Furthermore, all the study documents

were protected in a locked cabinet (paper based) and password protected computer files and these were only accessible to the investigators of this study. We notified the primary physicians attending the patient in cases we noted a child to be on low doses of medication or inappropriate AED according to seizure types. Also the primary physician attending the patient was notified if the child fulfilled criteria for IE, so that counseling and prompt management could be given.

All children continued to receive the best standard of care offered at MNH regardless of whether they accepted or decline to participate in this study

4.0 RESULTS

A total of 290 children with epilepsy who attended follow up at MNH pediatric neurology clinic during the study period were screened. Out of these 18.6 % were excluded because they either did not meet inclusion criteria due to short duration of treatment (<3months), young age or their guardians refused to provide written consent.



4.1 Social demographic and clinical characteristics of the study participants

A total of 236 patients with epilepsies attending pediatric neurology outpatient clinic were recruited to this study with male preponderance (56.4%). Median age of the participants was 72 months (IQR =42-78). At least two thirds of the participants were taken care of by their mothers whose majority had formal education except for only 10 (4.2%) with no formal education. About 9% reported to be using alternative therapies concurrently with AEDs

Table 1: Social demographic characteristics of the study participants).

Variable	**Category**	N	Frequency (%)
Age (Years)	1-3	73	30.9
	4-7	81	34.3
	8-11	50	21.2
	>12	32	13.6
Sex	Male	133	56.4
	Female	103	43.6
Primary care taker	Mother	155	65.7
	Father	5	2.1
	Both Parents	57	24.2
	Others*	19	8.1
Education of the care taker	No formal Education	10	4.2
	Primary School	106	44.9
	Secondary School	92	39
	Collage/ University	28	11.9
Consanguinity	Yes	7	3
Use alternative therapies**	Yes	22	9.3
	No	214	90.7

Others* include grand parents, aunt, siblings.

Alternative therapies**; included, local herbs, spiritual interventions .

The median age of onset of seizures was 7 months (IQR=1-24) with more than a quarter of the participants having their first seizure episode during the first month of life. Majority of the participants (60%) were on one AED. Self reported adherence was good (94.5%) and 89% of the participants had appropriate AED for seizure type. Only 38.6% were seizure free since their last optimization or change of AED. **(Table 2)**.

Table 2: Clinical Characteristics of the Study participants (N=236).

Variable	Category	N	Frequency (%)
Age of onset of seizures (Months)	<1	65	27.3
	1-12	79	33.5
	>12	92	39
Number of medications current using	One	143	60.6
	Two	73	30.9
	Three or more	20	8.5
Appropriateness of Anti Epileptic Medication for seizure type	Yes	210	89
	No	26	11
Adherence Bad adherence	Good	223	94.5
	Bad	13	5.5
Seizure Control Since last optimization/Change of Medications	Yes	91	38.6
	No	145	61.4

4.2 Prevalence of Intractable Epilepsy

As shown in **(Figure 2),** the prevelence of intractable epilepsy among children with epilepsies attending pediatric neurology out patient clinic was 14.8 , 95% CI (10.6-20.0)%.

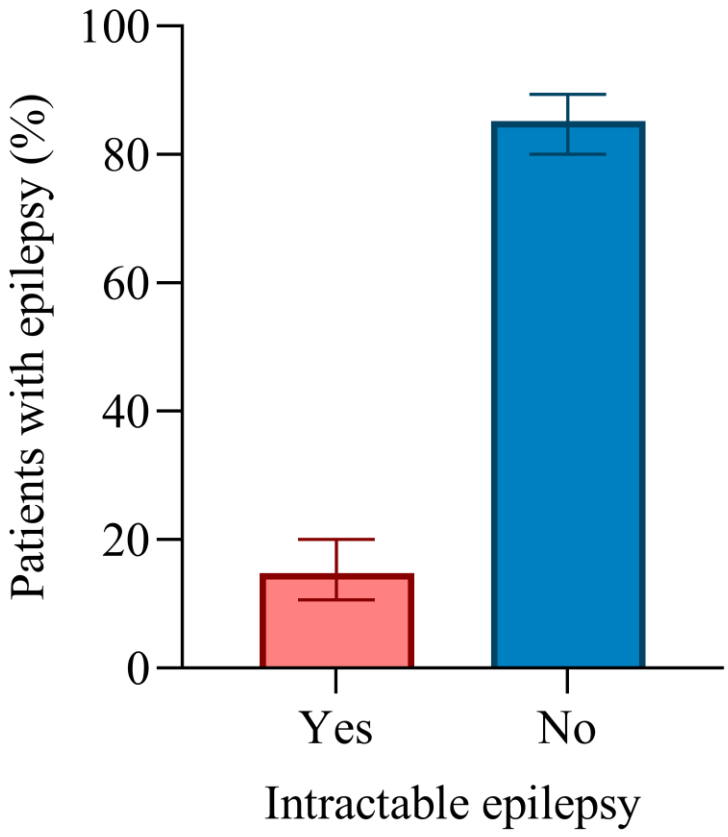


Figure 2. Prevalence of intractable epilepsy among study participants.

Clinical pattern of seizures among patients with intractable epilepsy.

Among patients with intractable epilepsy, majority (60%) had generalized epilepsies. Eight (23%) patients with intractable epilepsy had electro clinical diagnosis of epilepsy syndrome with Lennox Gaustat Syndrome being the commonest followed by West and Doose syndrome **(Table 3).**

Table 3: Clinical pattern of seizures among patients with intractable epilepsy attending neurology clinic at MNH.

Variable	Category	N	Frequency (%)
Seizure type	Focal	12	34.2
	Generalized	20	57.1
	Combined	3	8
Epilepsy type	Generalized	21	60
	Focal	11	31.4
	Combined	3	8.6
Epilepsy syndromes*	Yes	8	22.9
	Doose Syndrome	1	2.9
Syndrome type (N=8)	Lennox Gaustat Syndrome	5	11.4
	West Syndrome	2	5.7

Epilepsy syndromes*-Diagnosis was made based on types of seizures supplemented with typical EEG findings.

4.3 EEG and MRI findings among patients with intractable epilepsy attending pediatric neurology clinic at MNH.

Among patients with intractable epilepsy 80% had structural brain abnormality noted on MRI and almost a third had cystic encephalomalacia (34%) followed by brain atrophy (20.6 %). **(Table 4**)

Commonest structural lesions seen on MRI among patients with IE presenting with focal seizures were gliosis (noted in various areas of the brain) in 4 (36.4%) followed by brain atrophy and old ischemic changes respectively **(Figure 3).** Also 72% of the IE patients who presented with focal seizures had focal epileptiform discharges on EEG. **(Figure 4)**

Table 4: Neuro imaging and EEG findings among patients with intractable epilepsy. (N=35)

Variable	Category	Number	Percentage (%)
EEG	Normal	6	17.1
	Abnormal	29	82.8
MRI	Normal	7	20
	Abnormal	28	80
MRI abnormality (N=28)	Congenital anomalies	2	6.9
	Gliosis	6	20
	Cystic encephalomalacia	10	34
	Vascular (stroke)	2	6.8
	Hydrocephalus(post meningitis)	1	3.4
	Brain atrophy	6	20.6
	Mesial temporal lobe sclerosis	2	6.9

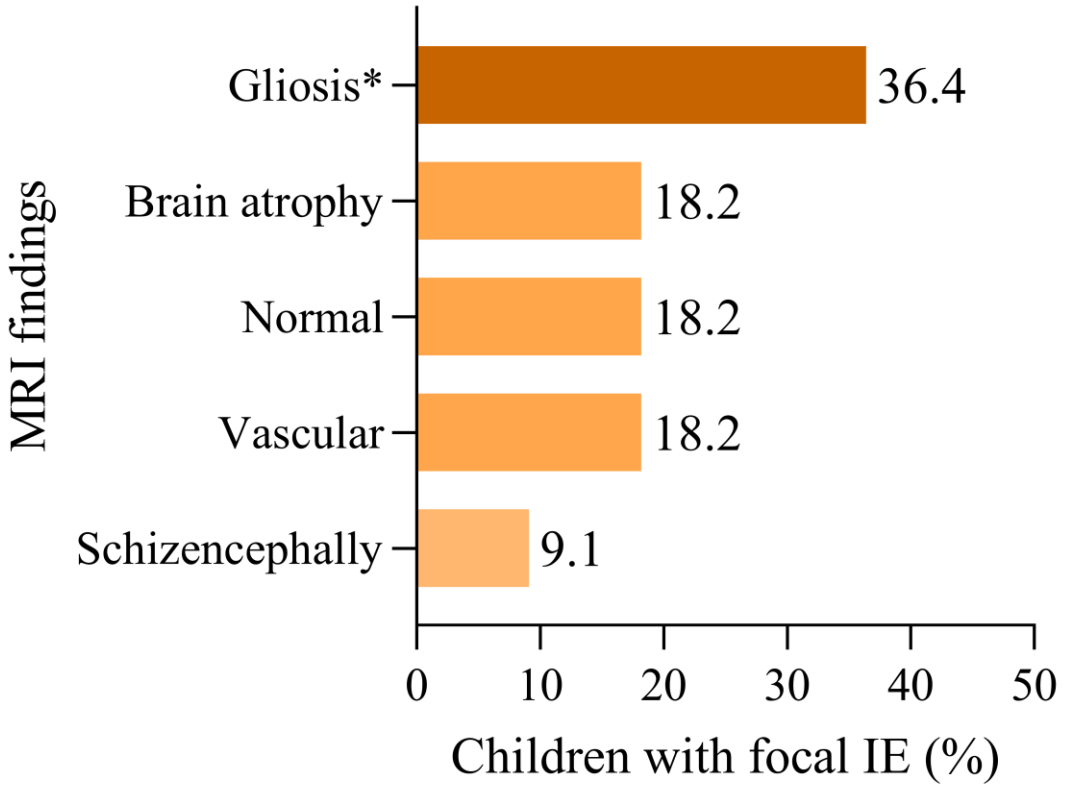


Figure 2: Distribution (%) of MRI findings among patients with intractable epilepsy who had focal seizures (N=11)

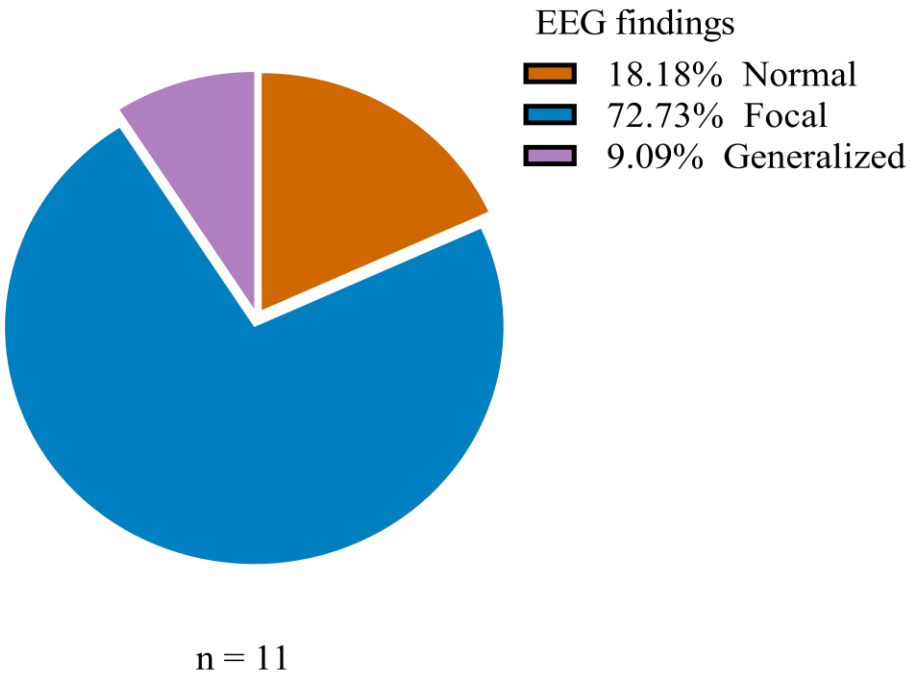


Figure 3: EEG findings (%) among patients with intractable epilepsy with focal seizures (N=11).

*Gliosis; Distribution of the lesion among the patients were as follows,

- Left occipital parietal gliosis noted in one patient
- Right sided extensive gliosis noted in one patient
- Occipital parietal gliosis in one patient
- Occipital gliosis in one patient.

4.4 Factors associated with intractable epilepsy among participants with intractable epilepsy attending pediatric neurology out patient clinic at MNH (N=236).

A large proportion of patients with intractable epilepsy had more than one seizure type at onset however the difference was not statistically significant (P=0.077). Other factors that were significantly associated with intractable epilepsy include high seizure frequency before treatment and global developmental delay. Similarly, large proportion of patients with intractable epilepsy had significant prior history of status epilepticus ($p<0.001$). Having a structural abnormality visible on brain MRI was found to be significantly associated with intractable epilepsy however EEG findings were not significantly associated with intractable epilepsy (P=0.281).

Table 5: Factors associated with intractable epilepsy among children with Epilepsy attending pediatric neurology clinic at MNH.

		INTRACTABLE EPILEPSY		
Variable	**Category**	**Yes%**	**No%**	**P value**
Sex	Male	20(15)	113(88)	0.9
	Female	15(14.6)	88(85%)	
Type of seizures at onset	1	24(12.8)	164(87.2)	0.077
	≥2	11(22.9)	37(77.1)	
Number of seizures at onset	< 10	12(27.7)	144(92.3)	<0.001
	≥10	23(28.7)	57(71.3)	
Delayed milestones	Yes	24(20.3)	94(79.7)	0.017
	No	11(9.3)	107(90.7)	
Neonatal seizures	Yes	16(25.8)	46(74.20)	0.007
	No	19(10.9)	155(89.1)	
Epilepsy syndrome	Yes	8(21.8)	30(78.9)	0.23
	No	27(13.6)	171(86.4)	
History of status epilepticus	Yes	20(27.4)	53(72.6)	<0.001
	No	15(9.2)	148(90.8)	
Consanguinity	Yes	1(14.3)	6(85.7)	0.31*
	No	34(14.8)	195(85.2)	
MRI (N=141)	Normal	7(12.1)	58(87.6)	0.003
	Abnormal	28(33.7)	83(66.3)	
EEG (N=169)	Normal	7(15.2)	39(84.8)	0.281
	Abnormal	28(22.8)	134(72.7)	

*Fisher's exact Test

4.5 Independent factors associated with intractable epilepsy among children with epilepsy attending pediatric neurology clinic at MNH.

High seizures frequency (more than 10) and onset of seizures during the first month of life were found to be independently associated with intractable epilepsy. Compared to those who had less seizure frequency, the odds of developing intractable epilepsy were 4.2 times higher as seizures frequency increases (OR=4.2; 95%CI 1.8-9.6;p=<0.001). Similarly the odds of developing intractable epilepsy among patients who had their first episode of seizure before one month of life was 2.8 times higher than those who had seizures later (OR=2.8; 95%CI 1-8.1;p=0.048)

Table 6: Independent factors associated with intractable epilepsy among patients with epilepsy attending pediatric neurology clinic at MNH.

		Univariate analysis			Multivariate analysis		
Variable	Category	COR	95% CI	P-value	AOR	95% CI	P-value
History of resuscitation	Yes	1.15	<0.01	0.1-0.2	1.96	0.2-15	0.52
	No	Ref					
Number of seizures at onset	>10	4.82	2.2-10	<0.001	4.2	1.8-9.6	<0.001
	≤10	Ref					
Seizure onset ≤1month	Yes	2.83	1.3-5.9	0.006	3.5	1.2-10	0.022
	No	Ref					
Global Developmental delay	Yes	2.3	1.15-5.34	0.02	2.2	0.8-6	0.20
	No	Ref					
History of status Epilepticus*	Yes	2.2	1.0-4.6	0.036	1.5	0.6-3	0.17
	No	Ref					

Statue epilepticus*- History of status epilepticus at any point since the onset of seizures.

5.0 DISCUSSION

Epilepsy is one of the common neurological disorders of childhood. This study aimed to determine the prevalence of intractable epilepsy and its associated factors among children with epilepsies attending neurology clinic at MNH. The ILAE 2010 definition of intractable epilepsy and 2017 ILAE seizures classification were used as current recommended standards. The prevalence of intractable epilepsy in this study was found to be 14.8%. This proportion is slightly lower but comparable to that observed in two studies involving Nigerian children where the prevalence was found to be 17.2% in a three year prospective study (28), and 19.9% in a two year retrospective study (45). Comparable findings from these two studies with this current study could be explained by similarities in etiology and risk factors for IE such as birth asphyxia and CNS infections in these two settings. Similarly, comparable rates (19%) were reported in Finland in a long term follow up of 37 years (6). Despite the difference in risk factors and duration of follow up between the Finish study and this current study, the prevalence of IE was comparable suggesting possibility of other intrinsic factors which were not assessed in the current study (genetic, structural and metabolic) that may predisposes an individual to intractable epilepsy (46).

In a long term follow-up Dutch study, involving children aged 1 month to 16 years who were newly diagnosed with epilepsy, 12% experienced a period of intractability during a 15-year follow-up since diagnosis and 8.5% remained intractable in the final year (47). Prevalence of IE from the Dutch study was lower compared to our study probably due to remitting relapsing course of IE. Intractable epilepsy may remit in the course of treatment if patients are followed up for a longer duration and hence the observed low prevalence in the Dutch study (6).

Furthermore, a retrospective study involving children diagnosed with epilepsy at age less than 2 years in Turkey, with at least 2 years of follow-up found that, nearly two thirds had drug-resistant epilepsy (48).

Involvement of children who were diagnosed younger than two years and methodology difference between the Turkish study and the current study partly explain the difference but also this might be due to a known risk of medical intractability among patients with early onset symptomatic epilepsies.

Findings from this study shows that, patients with intractable epilepsy were more likely to have generalized than focal epilepsies, findings which are in keeping with studies done in Malaysia (14) and India (49). In contrary studies done in developed countries found focal epilepsy to be more common than generalized epilepsy among patients with IE (26,29).This could partly be explained by etiological differences with adverse perinatal events which are associated with generalized epilepsy, being more common in resource limited settings like this study setting (50).

Neonatal onset seizures and history of higher seizure frequency before initiation of treatment were found to be independently associated with intractable epilepsy, similar to findings observed from other centers (25,34,35). Even though early insult to the brain might predispose patients to developing IE, evidence also suggest that early presentation might be an intrinsic characteristics of intractable epilepsies (19) and could be secondary to identifiable genetic causes and congenital structural malformation of the brain (51). These findings bring to our attention the importance of thorough evaluation, appropriate treatment and proper follow up of children with neonatal onset seizures.

Also a significant difference in occurrence of intractable epilepsy among patients with history of status epilepticus during the disease course was observed in univariate analysis but not in multivariate analysis. Recent evidence suggests status epilepticus to be a marker rather than a predictor of intractable epilepsy (13). Since this was a cross sectional study and caregivers reported events of status epilepticus, the possibility of recall bias cannot be excluded and hence loss of significance in multivariate analysis.

Observation from this study shows that, at least a quarter of patients with IE had epilepsy syndromes. Epilepsy syndromes are among the common causes of generalized intractable epilepsy in childhood (52). The commonest epilepsy syndromes found in this study were LGS followed by West syndrome, similar to what was observed in India and Netherlands (47,49). Some patients with West syndrome later on will develop LGS. The underlying causes of IE in these syndromes are cortical malformations, perinatal insults, chromosomal disorders and inborn errors of metabolism however some cases are cryptogenic (53).

Literature suggests that, combined therapy including medical, ketogenic diet and surgical intervention in some cases can have benefitting results among patients with Lennox Gaustaut syndrome and West syndrome (54,55).

Despite being difficult to manage, ketogenic diet among other alternative treatment have been found to improve outcome with up to 90% seizures reduction in patients with some epilepsy syndromes (56).

In this study eighty percent of all patients with IE were found to have structural lesions on brain MRI. Furthermore there was a significant relationship between abnormal MRI findings and occurrence of IE, similar to studies done in done in Turkey and USA (25,26). Cystic encephalomalacia, which commonly occurs as a result of perinatal ischemic or hypoxic insult, was the commonest structural abnormality observed among patients with intractable epilepsy. Thus despite the fact that history of resuscitation at birth was not found to predict intractable epilepsy, these findings suggests possibility of recall bias which led to underestimation of severe perinatal asphyxia among these patients.

Among patients with focal seizures who had intractable epilepsy in this study, more than half presented with abnormal neuroimaging findings, including gliosis (known to be potentially epileptogenic foci), schizencephally and ischemic infarcts all of which are possible candidates for epilepsy surgeries (23).

Surgical treatment for symptomatic focal intractable epilepsy offers a possibility of definitive cure and prevent neurocognitive sequel of recurrent seizures (57,58). Thus the observation from this study center where facilities for neurosurgery are available warrants further evaluation for possible curative or palliative epilepsy surgeries.

On the contrary, despite the observation of high proportion of patients with IE who had abnormal EEG finding, this was not found to be significantly related to IE, unlike in studies done in other centers (12,29). The inter ictal EEG in this study center are recorded only for 20-30 minutes and hence low less chances of picking epileptiform discharges. Also the interval between last seizures to the time of doing EEG might be prolonged given the logistical issues in this study center and hence decreases the yield. Further more since only conclusions of findings were available and not the actual tracings, the investigators could not exclude the possibility of inter observer variability.

5.1 Strength of the Study

- This was the first study done in Tanzania to assess the magnitude and predictors of IE and to the best of our knowledge, none have been published in literature from East Africa.
- The most recent ILAE recommended definition of intractable epilepsy and classification were used, making it easy to compare findings from this study with others from different centers.

5.2 Limitation of the study

- Causal association cannot be inferred given the cross sectional design of this study.
- Some of the variables inquired were subjected to recall bias; age of onset of seizures, seizures frequency, history of status epilepticus, perinatal and medications history. Measures were taken to mitigate including counter checking with patient's medical records.

6.0 CONCLUSION AND RECOMMENDATIONS.

6.1 Conclusion

Almost 15% of all patients with epilepsy attending pediatric neurology clinic were found to be intractable to medical management. Patients with IE were more likely to present with generalized epilepsy with one in every five having a clinical diagnosis of epilepsy syndrome. Also more than three quarters of patients with IE had an underlying structural brain abnormality.Independent factors associated with intractable epilepsy were neonatal onset seizures and high initial seizures frequency.

6.2 Recommendation

1. Alternative treatment such as surgery, ketogenic diet, VNS in this study setting should be considered given the high prevalence of IE.
2. A close follow up of patients with neonatal onset seizures and high seizure frequency is recommended given the higher preponderance to intractability among this group.
3. Patients with IE should have an imaging done given the higher prevalence of structural brain abnormalities among this group.
4. A longitudinal study is recommended to follow up patients found to have IE in order to obtain a more precise prevalence given the remitting relapsing course of intractable epilepsy.

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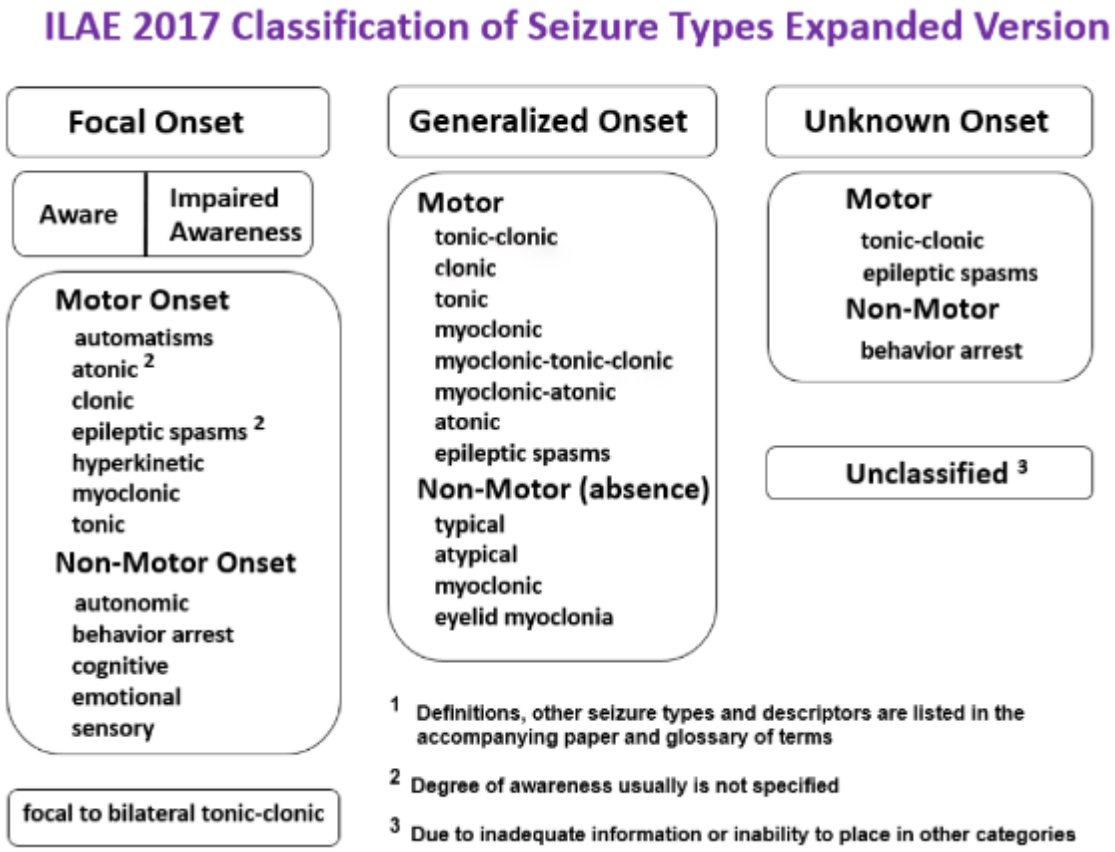
APPENDICES

Appendix 01- Classification of Seizures.



Appendix 02- Epilepsy Classification.

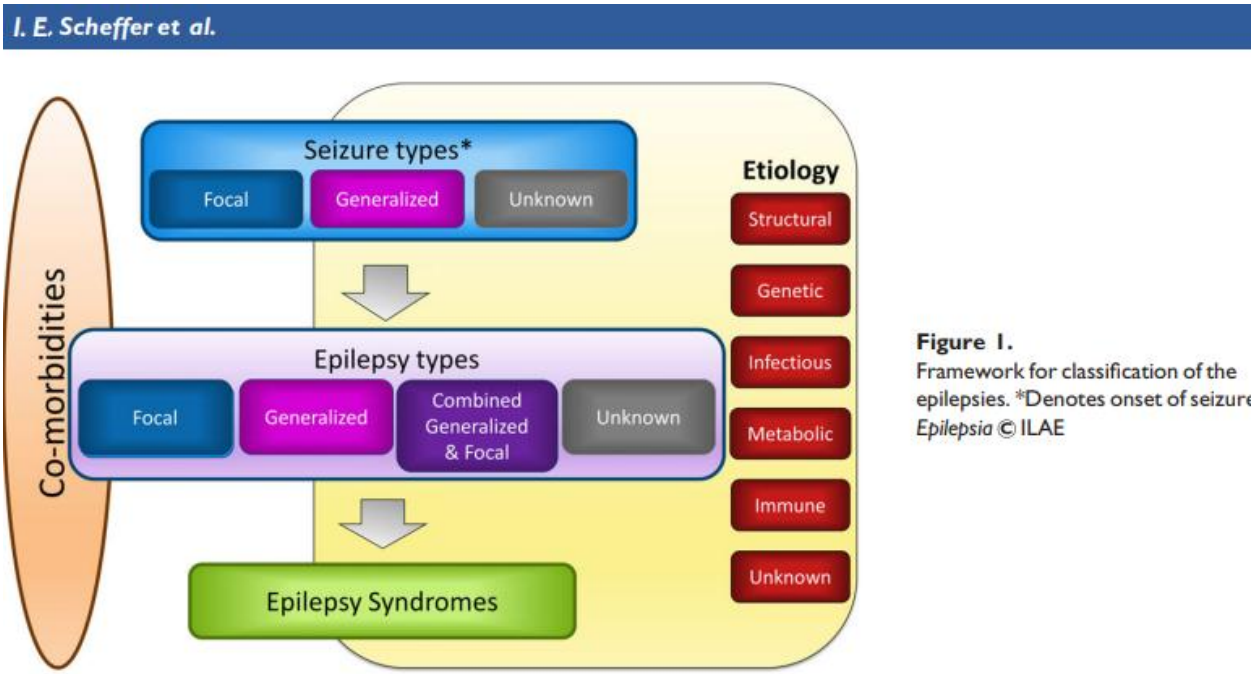


Figure 1.
Framework for classification of the epilepsies. *Denotes onset of seizure
Epilepsia © ILAE

Appendix 03: Questionnaire. English Version

MUHIMBILI UNIVERSITY OF HEALTH AND ALLIED SCIENCES

MAGNITUDE OF INTRACTABLE EPILEPSY AND ASSOCIATED FACTORS AMONG CHILDREN WITH EPILEPSY AGED BETWEEN 2MONTHS TO 15YEARS ATTENDING PEDIATRIC NEUROLOGY CLINIC AT MUHIMBILI NATIONAL HOSPITAL.

REF NO……

DEMOGRAPHIC CHARACTERISTICS

1. Date of birth DD/MM/YY ……../……../……
2. Weight (kg)……..
3. OFC (cm)…….
4. Length (cm)…….
5. Sex
    i) Male
    ii) Female
6. Ethnicity
    a) Indian
    b) African
    c) Arab
    d) Caucasians
7. Is the child attending school
    a) Yes
    b) No
8. If yes, in which grade is she/he …
9. If no, what is the reason for not attending school?
    a) Too young to go to school
    b) Fear of the disease occurring at school
    c) Prohibited by teachers

d) Prohibited by parents
e) Mocked by peers
f) Bullied at school
g) Others (Mention)…….

10. Who is responsible for taking care of the child?
    a) Mother
    b) Father
    c) Both parents
    d) Grand parents
    e) Others (specify)……
11. Age of the caregiver…
12. What is the level of Education of the caregiver?
    a) No formal education
    b) Primary education
    c) Secondary education
    d) University level
13. Are the parents related?.....
14. Who give the child his/her medications?
    a) Mother
    b) Father
    c) Siblings
    d) Grand parents
    e) Self
    f) Others (SPECIFY)…..
15. What is the level of Education of the treatment assistant?
    a) No formal education
    b) Primary education
    c) Secondary education
    d) University level

16. Occupation of the caregiver
    a) Employed
    b) Self employed
    c) Un employed
    d) Peasant
17. Is there any other family member with epilepsy/seizure disorder?
    a) Yes
    b) No
18. Are the seizures usually associated with fever?
    a) Yes
    b) No
19. If yes how is that patient related to the child
    a) Sibling
    b) Mother
    c) Father
    d) Uncle
    e) Aunt
    f) Grand parents
    g) Second degree relative
20. Age at onset of the seizures……..
21. Description of the seizures (using ILAE 2017-**DESSRIBE**) ……
22. From question 22 below to 30, Researcher/assistant will enter the best response based on the response obtained from above description,
23. Onset of seizure
    a) Focal onset
    b) Generalized onset
    c) Focal to bilateral
    d) Unknown Onset

24. For generalized seizures/Unknown onset
    a) Motor
    b) Non Motor
25. Generalized onset, **Motor seizures**
    a) Tonic
    b) Clonic
    c) Tonic Clonic
    d) Myoclonic
    e) Myoclonic-tonic-Clonic
    f) Myoclonic atonic
    g) Atonic
    h) Epileptic spasms
26. Generalized onset, **Non motor seizures**
    a) Typical absence
    b) Atypical absence
    c) Myoclonic absence
    d) Absence with eye lid myoclonia
27. For **focal onset** of the seizure, how was the awareness during the episodes
    a) Aware
    b) Impaired awareness
28. Focal onset, Motor seizures
    a) Automatisms
    b) Atonic
    c) Clonic
    d) Epileptic spasms
    e) Myoclonic
    f) Tonic

29. Focal onset, Non motor seizures
    a) Automatisms
    b) Behavior arrest
    c) Cognitive
    d) Emotional
    e) Sensory
30. Epilepsy syndrome
    a) Yes
    b) No
31. Syndrome name …….
32. Epilepsy type
    a) Focal
    b) Generalized
    c) Combined
    d) Unknown
33. Where was the patient taken during the initial attack?
    a) Hospital
    b) Alternative medicine
34. Overall performance of the child at school
    a) 80-100
    b) 79-60
    c) 59-40
    d) 39-30
    e) <30
35. Before the first episode of convulsions, did the patient had fever
    a) Yes
    b) No

36. Was there any history of convulsions during the neonatal period?
    a) Yes
    b) No
37. Was there delayed crying after birth
    a) Yes
    b) No
    c) I don't know
38. After how long was breast-feeding initiated?
    a) Within 1 Hour post delivery
    b) Within 24 hours but more than one hour
    c) More than 24 hours
39. Was resuscitation, requiring bag and mask done after delivery?
    a) Yes
    b) No
40. Was the child kept on oxygen after delivery?
    a) Yes
    b) No
41. For how long was the patient kept on oxygen (days).
42. Did the child have jaundice during the neonatal period?
    a) Yes
    b) No
43. When did the jaundice start
    a) Within the first 24hours after delivery
    b) After 24 Hours
44. How extensive was the jaundice
    a) Involved the eyes only
    b) Involved the face
    c) Face and all limbs
    d) Involve the entire body

45. Was the child kept on phototherapy?
    a) Yes
    b) No
46. Was there any history of Head trauma preceding the onset of seizures?
    a) Yes
    b) No
47. Is there any history of an episode of seizure that lasted more than 30 minutes
    a) Yes
    b) No
48. Is there any history of having two ore more episodes of seizures without regaining consciousness in between the episodes/Ho of being admitted to ICU due to un remitting seizures?
    a) Yes
    b) No
49. How long did it take (YY/MM) since the patient had the first episode of seizures to the initiation of anti Epileptic medications?……
50. Number of episodes of seizures per day before starting treatment ……
51. Types of medications that the patient is currently on (Drug(s), dose/kg, frequency) include other medication that were used in the past ……
52. How many types of anti epileptic medications is the patient currently on?
    a) One
    b) Two
    c) More than two
53. Was there any attempt to increase dose of the past three months since the medication was started
    a) Yes
    b) No
54. How long has it been since the optimization of the dose …….

55. Is there any change of medications since the patient started AED?
    a) Yes
    b) No
56. When were the medications changed (interval between previous and current medication …
57. Is the patient taking medication daily as per recommendations? (Consider last 5 days)
    a) Yes
    b) No
58. If the patient has discontinued medications, or is not using medications daily, what is the reason?
    a) Unsatisfactory seizure control
    b) Adverse effects
    c) Long term seizure freedom
    d) Economic reasons
    e) Others (mention) ……..
59. Is the patient still experiencing seizure despite being on AED?
    a) Yes
    b) No
60. If yes, how many per day/Month….
61. When was the last time this child experienced a seizure episode …..?
62. Is the child using any alternative treatment for the seizures?
    a) Yes
    b) No
63. What alternative treatment is the child using (examine if the child is wearing any)…….
64. Are EEG results present?
    a) Yes
    b) No
65. If yes, what were the findings?(diagnosis) ……..
66. What was the abnormality noted on the MRI……

67. Was there any developmental delay before seizures?

a) Yes
b) No

68. Was there developmental regression after seizures?

a) Yes
b) No

Developmental assessment

Chronological Age	Developmental Age	
	Before seizures	After seizures
Gross motor		
Fine Motor		
Speech And Language		
Social Behavior		

69. Intractable epilepsy

a) Yes
b) No

Appendix 04 Dodoso kwa Kiswahili

MAGNITUDE OF INTRACTABLE EPILEPY AND ASSOCCIATED FACTORS

REF NO……

1.UZITO……KG,

2.UREFU….CM.

3.OFC……CM

4. Tarehe ya kuzaliwa

DD/MM/YY

……../……../……

1. Jinsia
   i. kiume
   ii. kike
2. Asili
   i. Indian
   ii. African
   iii. Arab
   iv. caucasian
3. Je mtoto anakwenda shule?
   i. Ndio
   ii. Hapana
4. Kama anakwenda shule,Je anasoma darasa la ngapi?

   ……..
5. Kama jibu ni hapana kwenye swali la (4),je ni nini sababu ya mtoto kutohudhuria shule(Chagua yoye anayohusika)
   i. Umri mdogo kuanza shule
   ii. Hofu ya kupata degedee shuleni
   iii. Amekatazwa na walimu kutokana na ugonjwa
   iv. Amekatwazwa na wazazi kutokana na hali ya ugonjwa
   v. Anachekwa na wanafunzi wenzake
   vi. Anapigwa na wanzafunzi wenzake
   vii. Sababu nyinginezo(taja)……..……

   ……..
6. Je ni nani anamuhudumia mtoto?
   i. Mama
   ii. Baba
   iii. Wazazi wote kwa pamoja
   iv. Babu/Bibi
   v. Wengineo(taja)
7. Umri wa anayemuhudumia mtoto……
8. Kiwango cha elimu cha anayemuhudumia mtoto?
   i. Hajaenda shule
   ii. Eliumu ya msingi
   iii. Elimu ya sekondari
   iv. Elimu ya chuo

9. Kabila la wazazi

a) Mama……..

b) Baba……..

10. Je wazazi wa mtoto ni ndugu?

a) Ndio

b) Hapana

11. Nani anahusika kumpa dawa mtoto

a) Mama

b) Baba

c) Ndugu wa kuzaliwa

d) Babu/Bibi

e) Mtoto mwenyewe

f) Wengineo(taja)

12. Kiwango cha elimu cha anayehusika kumpa dawa mtoto

a) Hajaenda shule

b) Elimu ya msingi

c) Elimu ya sekondari

d) Chuo

e) Chuo kikuu

13. Kazi ya anayemuhudumia mtoto

i. Amejiajiri

ii. Ameajiriwa

iii. Hana Ajira

iv. Mkulima

14. Je kuna mwanafamilia mwingine mwenye ugonjwa wa kifafa?

i. Ndio

ii. Hapana

15. Kama yupo mwanafamilia mwenye kifafa,Je ni kila degedege anayopata inaambatana na homa?

a) Ndio

b) Hapana

16. Kama jibu ni ndio (swali namba 15),je ana uhusiano gani na mtoto?

a) Ndugu wa kuzaliwa

b) Mama

c) Baba

d) Mjomba

e) Shangazi

f) Babu/Bibi

17. Je mtoto alianza kupata degedege akiwa na umri gani……..

18. Description of the seizures (using ILAE 2017 DESCRIBE) Investigator will enter the information in English for question (19-28)use the lassification described in

19. appendix

    1……

    ……

20. Onset of seizure

    i. Focal onset

    ii. Generalized onset

    iii. Focal to bilateral

    iv. Unknown Onset

21. Onset of generalized seizures

    i. Motor

    ii. Non Motor

22. Generalized onset, Motor seizures

    i. Tonic

    ii. Clonic

    iii. Tonic Clonic

    iv. Myoclonic

    v. Myoclonic-tonic-Clonic

    vi. Myoclonic atonic

    vii. Atonic

    viii. Epileptic spasms

23. Generalized onset, Non motor seizures

    i. Typical absence

    ii. Atypical absence

    iii. Myoclonic absence

    iv. Absence with eye lid Myoclonia

24. For focal onset of the seizure, how was the awareness during the episodes

    i. Aware

    ii. Impaired awareness

25. Focal onset , Motor seizures

    26. Automatisms

    27. Atonic

    28. Clonic

    29. Myoclonic

    30. Tonic

31. Focal onset, Non motor seizures

    i. Automatisms

    ii. Behavior arrest

    iii. Cognitive

    iv. Emotional

    v. Sensory

32. Epilepsy syndrome

    i. Yes

    ii. No

33. Epilepsy type

    i. Focal

    ii. Generalized

    iii. Combined

    iv. Unknown

34. Je Mgonjwa alipelekwa wapi degedege ilipoanza?

    i. Hospital

    ii. Tiba mbadala

35. Nini matokeo ya ujumla ya ufaulu wa mtoto?
    i. 80-100
    ii. 79-60
    iii. 59-40
    iv. 39-30
    v. Pungufu ya 30

36. Je mtoto alikua na homa kabla ya kupata kupata degedege mara ya kwanza?
    i. Ndio
    ii. Hapana

37. Je kuna historia ya mtoto kupata degedege alipokua mchanga (Ndani ya mwezi mmoja toka kuzaliwa)?
    i. Ndio
    ii. Hapana

38. Je mtoto alichelewa kulia alipozaliwa?
    i. Ndio
    ii. Hapana
    iii. Sijui

39. Je mtoto aliweza kunyonya mwenyewe baada ya muda gani tangu alipozaliwa
    i. Ndani ya saa moja la kuzaliwa
    ii. Zaidi ya saa moja ila ndani ya saa 24
    iii. Zaidi ya saa 24

40. Je ,mtoto alihitaji kusaidiwa kupumua baada ya kuzaliwa?
    i. Ndio
    ii. Hapana

41. Je mtoto aliwekwa kwenye hewa ya Oxygen au mashine ya kupumulia baada ya kuzaliwa?
    i. Ndio
    ii. Hapana

42. Kama jibu (Namba 35) ni ndio,Je ilikua ni kwa siku ngapi?.....

43. Je mtoto alipata manjano wakati akiwa mchanga(ndani ya mwezi mmoja wa kuzaliwa)
    i. Ndio
    ii. Hapana

44. Kama jibu ni ndio(swali 39),Je manjano ilianza muda gani baada ya kuzaliwa
    i. Ndani ya saa 24 za kuzaliwa
    ii. Baada ya saa 24 za kuzaliwa

45. Je manjano ilikua kwenye maeneo gani ya mwili?
    i. Kwenye macho peke yake
    ii. Kwenye uso
    iii. Usoni Mpaka mikononi
    iv. Mwili mzima

46. Je mtoto aliwekwa kwenye Phototherapy?(taa yenye mwanga wa bluu)
    i. Ndio
    ii. Hapana

47. Je kuna historia ya mtoto kuumia kichwani na kupelekea kupoteza fahamu kabla ya mtoto kuanza kupata degedege??
    i. Ndio
    ii. Hapana
48. Je kuna historia ya mtoto kupata degedege kwa zaidi ya dakika 30 ?

a) Ndio
b) Hapana

49. Je kuna historia ya mtoto kupata degedege zaidi ya moja na bila kurudiwa na fahamu baina ya degedege moja na nyingine
    i. Ndio
    ii. Hapana
50. Je ilichukua muda gani tangu mtoto alipoanza kupata degedege kwa mara ya kwanza mpaka kuanzishiwa dawa za kifafa? ……
51. Kwa wastani,Mtoto alikua anapata degedege mara ngapi kwa mwezi kabla ya kuanzishiwa dawa za kifafa ……..?
52. Aina na dawa anazotumia mgonjwa sasa (information will be obtained from clinic visits from jeeva ™ ……...
53. Je dozi ya dawa ya mtoto ya kifafa imewahi kuongezwa tangu alipoanza matibabu
    i. Ndio
    ii. Hapana
54. Je ni muda gani umepita tangu dozi ilipoongezwa?.....
55. Je mtoto amewahi kubadilishiwa dawa tangu alipoanza matibabu ya kifafa?
    i. Ndio
    ii. Hapana
56. Je ni muda gani umepita tangu dawa zilipobadilishwa?.....
57. Je mtoto hunywa/hunywesha dawa zake kila siku kama ilivyoshauriwa na daktari?
    i. Ndio
    ii. Hapana
58. Kama jibu ni hapana (swali 54)Je ni nini sababu ya mtoto kuacha ama kutotumia dawa kila siku kama ilivyoshauriwa na daktari
    i. Matokeo ya matibabu yasiyo ridhisha
    ii. Madhara yatokanayo na dawa

iii. Kutopata degedege kwa muda mrefu
iv. Sababu za kichumi
v. Nyinginezo(taja)

59. Je mtoto amewahi kupata degedege hata baada ya dawa kubadilishwa/kuongezwa?
    i. Ndio
    ii. Hapana
60. Kama jibu ni ndio kwa swali 55,je kwa wastani mtoto anapata degedege mara ngapi kwa mwezi?……

61. Je ni muda gani umepita tangu mtoto alipopata degedege kwa mara ya mwisho?.....

62. Je mtoto anatumia tiba mbada kwa sasa?
    i. Ndio
    ii. Hapana
63. Ainisha tiba mbadala anayotumia mtoto kwa sasa……
64. What were the EEG findings?.....
    .....

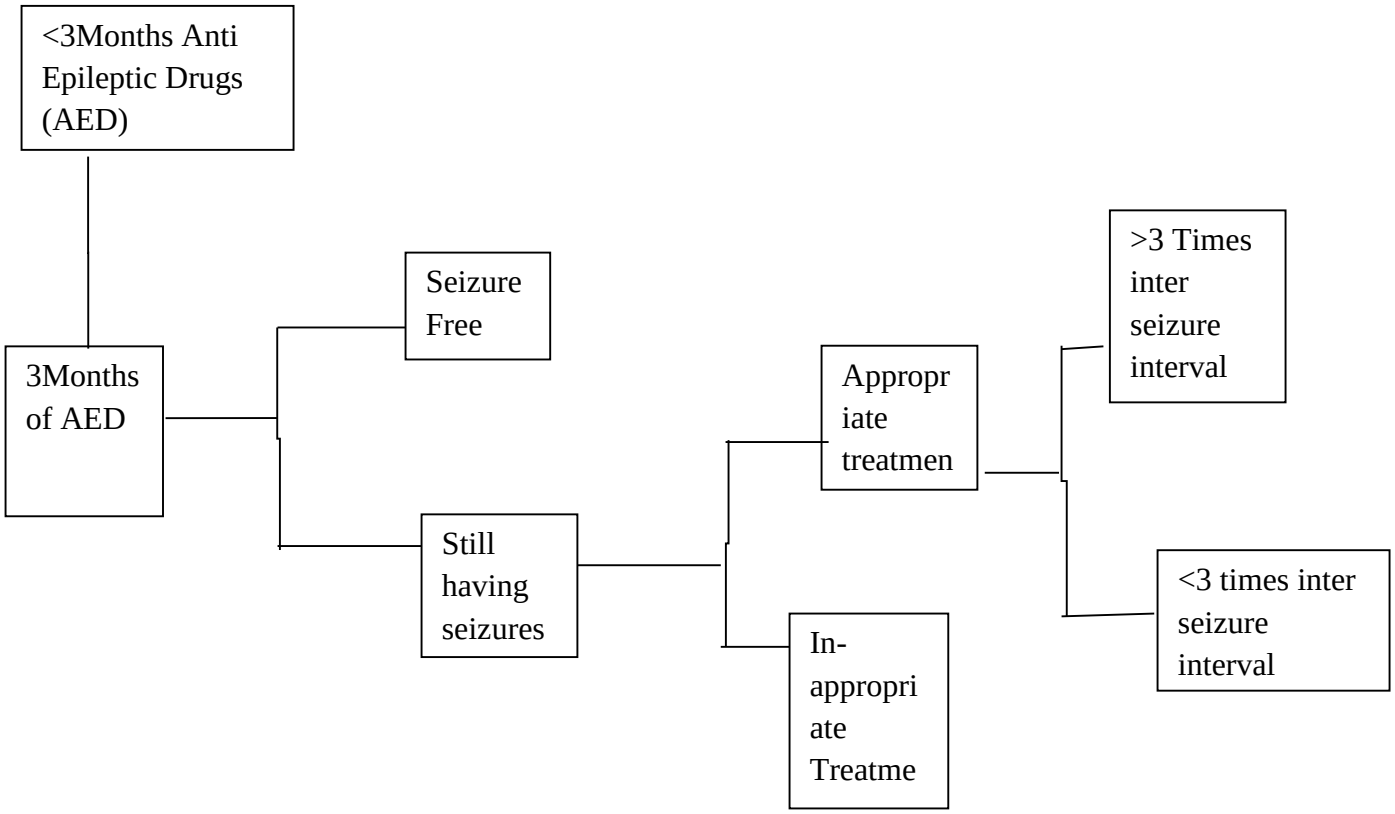
65. What was the abnormality noted on the MRI……

Chronological Age……	DEVELOPMENTAL AGE	
	BEFORE	AFTER
Gross motor		
Fine Motor		
Speech and Language		
Social Behavior		

66. Regression after seizures
    i Yes
    ii No
67. Delayed milestones
    i Yes

Appendix 05. Flow chart for classification of treatment response

This was attached in every questionnaire



Appendix 06. Consent form.

ID NUMBER……

MUHIMBILI UNIVERSITY OF HEALTH AND ALLIED SCIENCES (MUHAS)

An informed consent form for a study on Prevalence of intractable epilepsy and associated factors among patients with epilepsies attending pediatric neurology clinic at Muhimbili National Hospital

INTRODUCTION; My name is Dr. Obrey H Urio a resident at Muhimbili University of Health and Allied Sciences, Dar es Salaam. I'm doing a research on the magnitude, type of seizures, social demographic characteristics and other associated factors of intractable epilepsy among patients with epilepsy attending pediatric neurology clinic at Muhimbili National Hospital. I am going to give you information and invite you to be part of this research. Before you decide, you can talk to anyone you feel comfortable with about the research.

There may be some words that you do not understand. If you have questions, please ask me or any other doctor.

Purpose of the research: The purpose of this research is to determine the prevalence of intractable epilepsy and its associated factors so as to predict the risk of intractability in order for appropriate alternative treatment to be instituted before the adverse wide spectrum complications of repeated seizures can develop.

What does participation involves: This research will involve a questionnaire, which will assess the child if she/he qualifies to be enrolled in to the study. If you agree to participate in this study, you will be required to sign this consent form and then answer the questions in the questionnaire. It will take approximately 5 minutes of answering the question and a quick examination to the child including taking the occipital frontal circumference. You will also be required to provide the EEG report in case it was done before. If not MRI and EEG will be done as part of the standard of care in management of epilepsy.

Your participation in this research is entirely voluntary. Whether you choose to participate or not, all the services you receive at this hospital will continue and nothing will change. You may change your mind later and stop participating even if you agreed earlier.

CONFIDENTIALITY: Information about you and your child that will be collected during the research will be kept confidential and only the researchers will be able to see it. The identity of those participating in the research will not be revealed. In some circumstances we might discuss with your primary physician about the results and the medications in cases where we think improvements in the management is to be one.

RISKS: By participating in this research you will not face any risks.

There will be no any payments or compensations if you participate in this study, also you will not be required to pay in order to participate in this study

BENEFITS: This will help us to develop guidelines for diagnosis and treatment of intractable epilepsy and provide information to the policy makers so that alternative treatment modalities for intractable epilepsy can be instituted in our setting.

CERTIFICATE OF CONSENT: I have read the foregoing information, or it has been read to me. I have had the opportunity to ask questions and any questions that I have asked have been answered to my satisfaction. I voluntarily give consent for my child to participate as a participant in this research.

Name of Participant_____

Signature of Participant _____

Date _____

Day/month/year

IF A CAREGIVER IS ILLITERATE

A literate witness must sign (if possible, this person should be selected by the participant and should have no connection with the research team). Participants who are illiterate should include their thumbprint as well.

I have witnessed the accurate reading of the consent form to the potential participant, and the participant has had the opportunity to ask questions. I confirm that the participant has given consent freely.

Name of witness_____ AND Thumbprint of participant

Signature of witness _____

Date _____

Day/month/year

Appendix 07. Fomu ya ridhaa kwa mzazi

Namba ya utambulisho----------

UTAFITI KUHUSU KIFAFA SUGU ,NA SABABU ZAKE MIONGONI MWA WATOTO WENYE KIFAFA WANAOHUDHURIA KLINIKI YA WATOTO WENYE MAGONJWA YA MFUMO WA FAHAMU KATIKA HOSIPITALI TA TAIFA YA MUHIMBILI.

UTANGULIZI: Habari, naitwa Dkt Obrey H Urio, mwanafunzi wa shahada ya uzamili ya udaktari wa watoto katika Chuo cha afya na sayansi shirikishi cha Muhimbili.

Tunafanya Utafiti kuangalia ukubwa wa tatizo la kifafa sugu pamoja na visababishi vyake miongoni mwa watoto wenye kifafa wanaotibiwa katika kliniki ya watoto wenye magonjwa ya mfumo wa fahamu katika hosipitali ya taifa Muhimbili.. Nitakupa maelezo na kukualika kushiriki katika Utafiti huu, kabla ya kuamua unaweza kuongea na mtu yeyote kupata maelezo ya kutosha, kama kuna maneno hujaelewa vizuri unaweza kumwuliza daktari yeyote.

Lengo la huu utafiti: Lengo lake ni kutambua ukubwa wa tatizo la kifafa sugu pamoja na visababishi vyake miongoni mwa watoto wenye kifafa wanaotibiwa kama wagonjwa wa nnje katika hosipitali ya taifa ya Muhimbili. Hii itasaidia kutabiri uwezekano wa kifafa kua sugu mapema ili kupunguzu madhara yatokanayo na kupata degedege za mara kwa mara,pamoja na kushawishi uanzishwaji wa tiba mbadala kwa wagonjwa wenye kifafa sugu.

Kushiriki kutahusisha nini: Kama unakubali mwanao ashiriki katika Utafiti huu, tutakuuliza maswali kuhusu mwanao na familiayako. Mwanao atafanyiwa uchunguzi wa kumpima mzingo wa kichwa, na kuangalia kipimo cha MRI na EEG kama hajafanyiwa,ambavyo ni sehemu ya uchunguzi stahiki kwa watoto wenye kifafa sugu kadiri itakavyoshauriwa na daktari anayemuhudumia mtoto wako.

Kushiriki kwako ni kwa hiari na mwanao atapata huduma zote stahiki hata kama hutashiriki kwenye utafiti, pia kama baadae ukiamua kujitoa kwenye Utafiti mwanao ataendelea kupata huduma stahiki katika hosipitali ya Taifa Muhimbili.

Usiri wa taarifa: Taarifa zote zitakazopatikana katika utafiti huu zitabaki kuwa ni siri. Tutatumia namba ya hospitali na namba ya utambulisho ya utafiti kwa ajili ya kuwatambua washiriki wa utafiti, hakuna majina yatakayotumika katika utafiti huu au katika machapisho yoyote ya kiutafiti yatakayotokana na Utafiti huu hapo baadaye.

Majibu ya kipimo cha MRI na EEG yatajadiliwa na daktari bingwa wa mfumo wa fahamu kwa watoto na endapo atashauri kuboreshwa ka matibabu,basi taarifa hiyo atapewa daktari anayemuhudumia mtoto ili kuboresha matibabu.

Madhara ya kushiriki; Kwakushiriki kwenye Utafiti huu mwanao hatapata madhara yeyote.

Je, nitalipwa kwakushiki: Kushiki kwenye Utafiti ni hiari. Hakutakuwa na malipo kwa kushiki kwako kwenye utafiti. Pia hautahitajika kulipia chochote ili mwanao ashiriki katika utafiti

Tamko la ridhaa:

Mimi …… nimesoma yaliyomo kwenye hii fomu ya ridhaa, au nimesomewa yaliyomo kwenye hii fomu ya ridhaa. Maswali yangu yote yamejibiwa na nimepewa nakala ya hii fomu. Ninakubali kwa hiari yangu mwenyewe kuruhusu mwanagu ashiriki katika Utafiti huu

Saini ya mzami/mlezi ……. Tarehe: …….

Tamko la shahidi wamzazi/mlezi asiyejua kusoma au kuandika

Mimi……nimeshuhudia mzazi/mlezi wa mtoto akisomewa fomu hii ya ridhaa kwa usahihi. Mzazi/mlezi wa mtoto alipata nafasi ya kuuliza maswali ambayo yote yalijibiwa. Ninathibitisha kuwa mzazi/mlezi wa motto ameruhusu kwa hiari yake mwanae ashiriki katika utafiti.

Saini ya shahidi ……..……. Tarehe:…….

Dole gumba la mzazi/mlezi

Appendix 08.Assent form in English

Title: Magnitude of intractable epilepsy and associated factors among children aged six months to fourteen years attending neurology clinic at Muhimbili National Hospital

Hello, I am Dr Obrey H Urio, a resident in Paediatrics and Child Health department conducting a research on Magnitude of intractable epilepsy and associated factors among children with epilepsy attending pediatric Neurology clinic at Muhimbili National Hospital Dar es salaam Tanzania.

A research is a way to learn about people and if you decide you want to be a part of this study, you and/or your caregiver will be asked a few questions. If you do not want to be in this research, you will continue to receive the treatment and care that you need.

The reports and documents will not have your identity on it and whatever information you give us will be kept confidential.

You do not have to be in this study if you do not want to. If you decide to stop after we begin it is okay also.

If you decide you want to be in this study, please sign your name.

I, ---------- want to be in this study.

---------- ----------

Sign your name here Date

Namba ya utambulisho----------

KICHWA CHA HABARI. UTAFITI KUHUSU KIFAFA SUGU ,NA SABABU ZA USUGU MIONGONI MWA WATOTO WENYE KIFAFA WANAOHUDHURIA KLINIKI YA WATOTO WENYE MAGONJWA YA MFUMO WA FAHAMU KATIKA HOSIPITALI TA TAIFA YA MUHIMBILI

Habari, naitwa Dkt Obrey H Urio, mwanafunzi wa shahada ya uzamili ya udaktari wa watoto katika Chuo cha Sayansi Shirikishi cha Muhimbili.

Tunafanya utafiti kuangalia ukubwa wa tatizo la kifafa sugu na visababishi vyake miongoni mwa watotot wenye tatizo la kifafa wanaohudhuria kliniki ya watoto wenye magonjwa ya mfumo wa fahamu katika hosipitali ya taifa ya Muhimbili .Nitakupa maelezo na kukualika kushiriki katika utafiti huu, kabla ya kuamua unaweza kuongea na mtu yeyote kupata maelezo ya kutosha, kama kuna maneno hujaelewa vizuri unaweza kumwuliza daktari au muuguzi yeyote.

Utafiti ni njia ya kujifunza juu ya watu na ikiwa unaamua unataka kuwa sehemu ya utafiti huu, wewe na/au mlezi wako ataulizwa maswali machache. Unaweza pia kuhitaji kipimo cha MRI na EEG (kipimo cha ufanyaji kazi wa mfumo wa umeme kwenye ubongo) ,ambavyo ni sehemu ya uchunguzi stahiki kwa wagonjwa wenye kifafa.

Ikiwa hutaki kuwa katika utafiti huu, utaendelea kupata matibabu na huduma unayohitaji. Ripoti na nyaraka hazitakuwa na utambulisho wako juu yake na taarifa yoyote unayoyotoa itachukuliwa siri. Ni hiari yako kuwa katika utafiti huu na ikiwa hutaki hutalazimishwa hutaki. Ikiwa utaamua kuacha baada ya kuanza, hiyo ni sawa pia.

Ikiwa unaamua unataka kuwa katika utafiti huu tafadhali saini jina lako.

Mimi, ---------- nataka kuwa katika utafiti huu.

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Andika jina lako hapa Tarehe