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St. Paul's Hospital Millennium Medical College

**CLINICAL CHARACTERISTICS, OUTCOME, AND FACTORS
ASSOCIATED WITH MORTALITY IN PATIENTS WITH STATUS
EPILEPTICUS AT SELECTED PUBLIC HEALTH HOSPITALS IN
ADDIS ABABA, ETHIOPIA**

BY

Dr. MIHIRET LEGESSE (Internal medicine resident)

**A RESEARCH THESIS TO BE SUBMITTED TO SPHMMC, FACULTY OF PUBLIC
HEALTH, AND INTERNAL MEDICINE DEPARTMENT IN PARTIAL
FULFILLMENT OF THE REQUIREMENT FOR POST GRADUATE PROGRAM
OF INTERNAL MEDICINE.**

FEBRUARY, 2024

ADDIS ABABA, ETHIOPIA

ST PAUL'S HOSPITAL MILLENNIUM MEDICAL COLLEGE

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MIHIRET LEGESSE (Internal Medicine Resident)

ADVISORS:

- 1. Dr. TESFAYE BERHE (MD, CONSULTANT INTERNIST, NEUROLOGIST)**
- 2. Mrs. SISAY TANIE (MSc, BIOSTATISTICIAN)**

FEBRUARY, 2024

ADDIS ABABA, ETHIOPIA

St. Paul's Hospital Millennium Medical college

Graduate study program

Name of investigator	Dr Mihiret Legese (Internal Medicine Resident)
Full title of the research project	Clinical Characteristics, Outcome, And Factors Associated with Mortality in Patients with Status Epilepticus at Selected Public Health Hospitals in Addis Ababa, Ethiopia
Study Duration	April to June 2023
Study Area	St. Paul's Hospital Millennium Medical College, Tikur Anbessa Specialized Hospital and Aabet Hospital
Address of investigator	Tel: +251 974 078915 Email: mihiretlegese25@gmail.com
Name of Advisor(s)	Dr Tesfaye Berhe (MD, Neurologist) Mrs. SisayTanie (MSc, Biostatistician)

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ABBREVIATIONS

SE - Status epilepticus

AED - Antiepileptic drug

CSE- Convulsive Status epilepticus

RPCs – Resource Poor Countries

ILAE - International League Against Epilepsy

NHDS- National Health Discharge Survey

NCSE - Non-convulsive status epilepticus

RSE - Refractory status epilepticus

SRSE - Super-refractory status epilepticus

TASH- Tikur Anbessa Specialized Hospital

SPHMMC - Saint Paul Hospital Millennium Medical College

ABSTRACT

Background: Status epilepticus is a severe neurological emergency condition characterized by continuous, generalized convulsive seizure lasting for more than 5 minutes or two or more seizures without regaining consciousness. It is frequently associated with high death and morbidity rates.

Objective: To assess the clinical profile and in hospital outcome and associated factors of patients with convulsive status epilepticus among patients at St. Paul's Hospital Millennium Medical College, Tikur Anbessa Specialized Hospital and Aabet Hospital in Addis Ababa Ethiopia January 1, 2019 to September 30, 2022.

Methods: Retrospective cross-sectional descriptive study was carried out on the medical records of on 224 SE patients admitted to three public hospitals in Addis Ababa during the study period. For data analysis SPSS version 26 was used. Multivariate logistic regression analysis was performed to determine associated factors of poor outcome. The results were presented using tables, graphs and pie chart. All tests with P-Value <0.05 were considered statistically significant.

Results: Mean age was 37.8 years with 53.3% females. Pre-existing epilepsy was 34.4%. Major SE etiologies were stroke (20%), antiepileptic drug withdrawal (17.8%), central nervous system infections (13.3%), and brain tumors (12.2%). Over 50% had complications, largely aspiration pneumonia. Case fatality rate was 17.4%. Mortality predictors were HIV/AIDS with CNS complications (AOR 3.50, 95% CI 0.97-18.75), CNS infections (AOR 4.61, 95% CI 0.99-21.33) and having ≥ 2 complications (AOR 10.50, 95% CI 1.44-76.28).

Conclusion: Stroke, infections and drug non-compliance were major SE causes. Case fatality was high, associated with CNS infections and complications. The study highlights that non-communicable diseases like stroke are emerging as major contributors, while preventable causes like treatment non-compliance and infections continue to play a significant role in status epilepticus.

Recommendations: Guideline implementation, EEG access, medication compliance promotion, infection control and complication prevention should be prioritized to improve SE outcomes. Further studies on semiology and larger datasets could strengthen evidence.

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INTRODUCTION

1.1. Background

Epileptic status, also known as status epilepticus (SE), in adults is defined as continuous, generalized convulsive seizure that lasts for more than 5 minutes or two or more seizures during which the patient doesn't regain consciousness; is a severe neurological emergency condition that occurs frequently [1-3] and is associated with a high death and morbidity rate. There have been reports of fatalities in as many as 20% of cases, and morbidities in as many as 39%. [4]

There is a first peak in prevalence and incidence of SE during early childhood, and there is a second peak in older subjects, which is sometimes characterized as individuals who are above the age of 60 years. [5, 6] It is anticipated that the mean annual incidence rate is somewhere around 15.5/100,000 in patients who are between the ages of 60 and 69, 21.5/100,000 in patients who are between the ages of 70 and 79, and 24.9/100,000 in patients who are more than 80 years old. [7-9]

In adults who were diagnosed with SE, the most common causes were reported to be the discontinuation of antiepileptic medicines (AED) or an acute symptomatic etiology, most commonly an acute stroke. [6, 10] Patients do not have a history of earlier seizures or a diagnosis of epilepsy in the initial episode of SE in approximately fifty percent of cases. [9] These patients have a high risk of having new-onset refractory status epilepticus, which can have a negative impact on the outcome of their condition in up to fifty percent of the instances. [11] Interestingly, in nearly 20% of the cases the etiology is un-known. [4]

In a significant number of patients with pre-existing epilepsy, no precipitating factor has been reported. The short-term mortality (at 30 days) in CSE patients is approximately 27%. [12, 13] Patient age at diagnosis, severity of the etiology and duration of CSE has been shown to predict short-term mortality in these patients. [14, 15] Additionally, longer duration of SE may aid in making it refractory to treatment. [16] Importantly, early and aggressive management of CSE will improve outcome in these patients. [17] Knake et al, suggested that treatment of SE can be divided into three stages, initial out of hospital, initial treatment in hospital and treatment of RSE. [18] Various findings reported from large in hospital studies done in developed countries, show a variable prognosis of CSE, [19] with mortality ranging from 3% to 50%. However similar data in developing countries is scarce or under-estimated.

[15] Older age and CNS infections in children have been widely accepted predictors for poor outcome in patients with CSE. [4]

1.2. Statement of the problem

In resource-poor countries (RPCs), which are defined by the World Bank as low-income or middle-low-income countries, status epilepticus is a common occurrence among patients admitted to hospitals. However, there are disparities in the epidemiology, etiology, and outcome of status epilepticus in RPCs compared to high-income countries, and limited data is available from the former regions. The ILAE definition of status epilepticus is problematic in RPCs due to the absence of adequate documentation of the duration of convulsions at health facilities. Hence, alternative definitions have been proposed. Most studies in RPCs focus on convulsive status epilepticus, as nonconvulsive status epilepticus is rarely detected in these regions. The incidence of convulsive status epilepticus appears to be higher in RPCs than in high-income countries, with acute symptomatic seizures being more common in children, particularly in RPCs, and often leading to an increased incidence of epilepsy. The higher incidence of symptomatic convulsive status epilepticus is attributed to the higher incidence of infections, such as malaria and bacterial meningitis or viral encephalitis. The mortality associated with convulsive status epilepticus in RPCs is greater, with poor long-term outcomes, including increased risk of premature mortality and neurocognitive sequelae. The limited availability of drugs and inadequate healthcare facilities further complicates the treatment of convulsive status epilepticus in RPCs.[20]

CSE is a major public health problem and its incidence is estimated to be up to 40 cases per 100,000 people per year. In developing countries like Ethiopia, the incidence of CSE is higher due to the high prevalence of infectious diseases, malnutrition, and lack of access to adequate medical care. Furthermore, the management of CSE is often inadequate in many developing countries, leading to poor outcomes and increased mortality rates.[21]

The management of CSE involves prompt recognition, cessation of the ongoing seizure, and initiation of appropriate anticonvulsant therapy. The choice of anticonvulsant therapy should be based on the underlying cause of the seizure and the patient's age, comorbidities, and response to previous treatments. Despite the availability of effective anticonvulsant therapy, CSE often leads to severe neurological and cognitive sequelae, and the long-term outcome of patients with CSE remains unclear.[22]

Although previous studies investigated the clinical profile and outcomes of CSE patients in Ethiopia, they were based on an outdated definition of the condition. In 2015, the ILAE

proposed a new definition that emphasizes the importance of prompt treatment and better management. However, research on the clinical profile, outcome, and associated factors of patients with CSE using the updated definition is limited, particularly in Ethiopia. The purpose of this study is to fill that gap by investigating the clinical profile, outcome, and associated factors of CSE patients at selected public health hospitals in Addis Ababa, Ethiopia. The findings of the study help to improve understanding of CSE in the Ethiopian context, as well as inform healthcare providers on how to better manage CSE patients and reduce the burden of morbidity and mortality associated with the condition. As a result, the study is significant for filling a critical knowledge gap and advancing the field of epilepsy research.

1.3. Significance of the study

This study on the Clinical characteristics, Outcome, and factors associated with mortality in patients with status epilepticus in selected public health hospitals in Addis Ababa, Ethiopia, holds great significance in the field of medical research. The high burden of epilepsy in Ethiopia, with a prevalence rate of 64 per 100,000 populations in the general population and a high incidence of convulsive status epilepticus,[23] a life-threatening condition, calls for a comprehensive study that sheds light on this issue.

The outcome of this study holds immense potential to bring about improvement in patient care and outcomes. The identification of the clinical profile, outcome, and factors associated with mortality in patients with status epilepticus can serve as a basis for the development of evidence-based clinical practice guidelines, leading to an improvement in the quality of care provided to patients. The results of this study can also inform future research aimed at better management of convulsive status epilepticus in Ethiopia and similar settings.

Moreover, this study has the potential to increase awareness about the impact of convulsive status epilepticus on patients and their families, and to advocate for increased resources for the management of epilepsy and other neurological conditions in Ethiopia. Additionally, the study also helps to uncover disparities in access to care, treatment practices, and outcomes, thus informing efforts to address these issues and ensure equitable access to care for all patients with convulsive status epilepticus.

In conclusion, this study aims to provide valuable insights into the clinical characteristics and outcome of patients with CSE in Ethiopia. The findings of this study will help to improve the management of CSE in Ethiopia and potentially contribute to the reduction of the high morbidity and mortality associated with this condition.

2. LITERATURE REVIEW

In a 2008 study conducted in Ethiopia by Amanuel Amare et al., data from 119 patients with status epilepticus (SE) were evaluated to determine the clinical presentation, etiology, outcomes, and predictors of mortality. The mean duration of SE at arrival was 44.7 hours, while the median duration was 24 hours. The average hospital stay for the 56 patients admitted to the Medical Intensive Care Unit was 20.3 days. CNS infections were the most common cause of SE (36.1%), followed by antiepileptic medication noncompliance (17.6%) and idiopathic (16.1%). The study discovered that prompt diagnosis and treatment of SE is essential, particularly in resource-limited settings when patients present with a long duration of SE, which increases the risk of morbidity and mortality. [24]

Mahlet Abayneh's 2016 study sought to examine the demographic and clinical characteristics, causes, and short-term outcomes of infants with status epilepticus (SE) hospitalized to the Tikur Anbessa Specialized Hospital in Addis Ababa, Ethiopia. In a 5-year retrospective cross-sectional study conducted between January 2005 and January 2010, 89 children aged one month to thirteen years were evaluated. Male patients made up 58.4% of the sample, and 76.4% of the patients were from Addis Abeba, according to the results. The most prevalent form of seizure was generalized (74.2%), and idiopathic/cryptogenic reasons were the most common cause of SE (40.4%). Pyogenic meningitis was the most prevalent acute symptomatic etiology (20.2%), but prenatal injury was suggested in 12.4% of distant symptomatic cases. In infants younger than 12 months, acute symptomatic SE was the most prevalent (55%) whereas idiopathic/cryptogenic SE was the most prevalent in older children (96.7%). A past history of seizure was documented in 61.8% of patients, and 57.3% of these patients were released with no complications. However, 36.0% of patients had a neurologic deficit, and 6.7% of patients died, with higher rates of neurologic sequelae in younger children.[25]

László Horváth et al. conducted a prospective cross-sectional study to examine the outcome of status epilepticus (SE) and its long-term follow-up. They discovered that the prevalence of SE was 9.4-14.7/100,000 inhabitants per year, with the highest incidence in December and January, followed by August. 73.6 percent of the patients had a history of epilepsy, and 89 percent of those patients had symptomatic epilepsy. In patients with known epilepsy, infections, stroke, drunkenness, and noncompliance accounted for the majority of SE cases. Just under 50 percent of instances were focal, whereas 34.8% were widespread. All known

patients with epilepsy were using antiepileptic medicines (AEDs), however the pattern of AED use among SE patients differed significantly from those in outpatient care. In 17% of patients, general anesthesia was required. The study emphasizes the significance of effective epilepsy management with regular supervision and quick medication to prevent SE; it suggests additional research to enhance long-term results for SE patients. [26]

M. Hidalgo de la Cruz et al. conducted a study to identify risk factors for mortality in individuals with status epilepticus (SE) and to evaluate SE therapy. The study included 65 patients, with a mean age of 59 years and 53.8% females. 46.2% of patients had a history of epilepsy, and 53.8% were getting regular antiepileptic medication (AED) treatment, with levetiracetam being the most frequently administered AED. Patients receiving three or more AEDs had a greater risk of SE episodes than those receiving two or less AEDs, according to the study. The most common type of SE was generalized convulsive SE, with structural impairment to the central nervous system (CNS) and a lowered seizure threshold as the underlying reasons. The causes of structural damage were cerebrovascular events and primary CNS malignancies, whereas the causes of lowered seizure threshold were systemic infection and missed doses of routine AEDs. In the acute phase of SE, benzodiazepines were the most prevalent treatment, with diazepam being the most common, although clonazepam had a higher percentage of cases of SE termination. In 46.2% of cases, the study detected modifications from standard treatment, such as the use of two distinct benzodiazepines, the substitution of an AED for benzodiazepines, and the off-label use of lacosamide. The study underscores the necessity of regular AED treatment and quick treatment with appropriate AEDs to control seizures in epilepsy patients in order to prevent SE.[27]

Rahul Rathakrishnan, NovaliaPurnamaSidik, Chan YiongHuak, and Einar P. Wilder-Smith conducted a study on 62 adult patients admitted to the National University Hospital in Singapore from 2002 to 2005 to investigate the characteristics, outcomes, and potential prognostic markers of convulsive status epilepticus (SE). The results showed that the mean duration of seizures was 98.7 minutes, and 82% of patients had ongoing seizures upon arrival in the emergency department. Structural brain abnormalities were detected in 93% of the patients who underwent neuroimaging, and hyperglycemia was identified as a novel prognostic marker when combined with age. The ROC of the constructed model was 0.817. the study highlights similarities and differences with other reports on SE and emphasizes the possibility of different populations showing different indicators of poor prognoses. The study

also identified hyperglycemia as a novel prognostic marker in the Singaporean population.[28]

Sebastián Sánchez and Fred Rincon conducted a literature review on Status Epilepticus (SE) focusing on epidemiology and public health needs. After eliminating duplicates, 55 articles met the criteria, with 49 used for the final review. The National Health Discharge Survey (NHDS) in the U.S. showed SE accounted for 0.07% of hospital admissions over 32 years (1979-2010) with equal gender distribution and a higher incidence in males, showing a bimodal distribution with peaks in the first decade of life and after 60 years. Studies in North America, Asia, Europe, and Africa showed similar bimodal distribution with increased incidence in the elderly and a male preponderance. In children, the major cause of SE is infection with fever, while in adults it is low anticonvulsant levels, remote symptomatic epilepsy, and stroke. In the elderly, the major cause is cerebrovascular accident. Comorbidities such as diabetes, hypertension, trauma, acute cardiac/respiratory events, hepatic decompensation, epilepsy, and dysnatremia are significantly associated with SE in the elderly. The authors highlight the need for better understanding of the epidemiology and risk factors to improve public health measures and outcomes. With a projected increase in the elderly population, the authors emphasize the need for continued research to address the growing public health issue of SE.[29]

The study by Lichao Sun, Chuntao Han, and Weihong Lin aimed to investigate the clinical characteristics and prognosis of status epilepticus (SE) in Northeast China, retrospectively analyzing the clinical profiles of 223 patients diagnosed with SE at the Epilepsy Center of Jilin University between 2011-2015. The causes of SE were diverse and epilepsy was the most common, accounting for 47.53% of the cases. The mortality rate was 6.73% with multiple organ dysfunction syndrome being the major cause of death. Old age and non-convulsive status epilepticus (NCSE) were found to be risk factors for potential progression to refractory status epilepticus (RSE) or super-refractory status epilepticus (SRSE), while central nervous system infection, autoimmune encephalitis, and epilepsy were common causes of SE but showed no significant association with the risk of progression into RSE.[30]

The study conducted by Pan et al. aims to compare the clinical characteristics and outcomes of patients diagnosed with status epilepticus (SE) at two distinct time points, t1 and t2, as proposed by the International League Against Epilepsy in 2015. A prospective observational cohort study was carried out with 100 adults diagnosed with SE, and data on demographic,

clinical, and outcome measures were collected. The results revealed that 56% of the participants reached t1, while 44% reached t2 of SE, with convulsive SE being more common than focal SE with impaired consciousness. The study found that patients who reached t2 of SE had a significantly increased risk of mortality and unfavorable functional outcomes at 3 months post-onset, as compared to those who only reached t1 of SE. Additionally, seizure recurrence was observed more frequently among patients reaching t2 of SE. [31]

The study by Sudhindra Vooturi et al. aimed to determine the clinical characteristics and factors associated with in-hospital mortality in adult patients admitted to the neuro intensive care unit (NICU) with convulsive status epilepticus (SE). Acute symptomatic etiology was the most common cause of SE in adults, with an increased risk of mortality 5.28 times higher compared to other etiologies. The study revealed that the requirement for mechanical ventilation and refractory SE were the major factors associated with mortality. These findings suggest that prompt recognition and management of acute symptomatic etiology as well as effective treatment for complications such as prolonged mechanical ventilation and refractory SE are crucial in reducing mortality among adult patients with SE.[32]

A study was done in Mogadishu, Somalia to understand the epidemiology, risk factors, and outcomes of convulsive status epilepticus (SE) patients in a tertiary hospital's ED. Conducted between 2021-2022, the study included patients with and without epilepsy, with the average age being 6 years for pediatric patients and 38 years for adults. 36% of patients had prior epilepsy, while 64% had their first seizure in the ED. 87% had generalized seizure, while 13% had focal seizure. The most common risk factor was poor antiepileptic drug compliance, followed by CNS infections and prolonged febrile seizures. In adults, poor antiepileptic compliance, cerebrovascular disorders, electrolyte imbalances, metabolic conditions, and drug abuse were the leading causes. In children, the leading causes were prolonged febrile seizure, meningitis, encephalitis, systemic infections, and structural brain abnormalities. The main risk factors for SE in patients without prior epilepsy were CNS infections, cerebrovascular disorders, metabolic disturbances, electrolyte imbalances, and systemic infections, while medication adherence was the main factor in patients with epilepsy.[33]

3. OBJECTIVES OF THE STUDY

3.1 General Objective

- ✓ To assess the clinical characteristics, hospital outcome and factors associated with mortality in patients with status epilepticus, among patients at St. Paul's Hospital Millennium Medical College, Tikur Anbessa Specialized Hospital and Aabet Hospital in Addis Ababa, Ethiopia from January 1, 2019 to September 30, 2022.

3.2 Specific Objectives

- ✓ To assess the sociodemographic characteristics of patients with status epilepticus
- ✓ To identify the clinical characteristics of patients with status epilepticus
- ✓ To assess hospital outcome of patients with status epilepticus
- ✓ To assess associated factors of the mortality in patients with status epilepticus

4. METHODOLOGY (METHODS AND MATERIALS)

4.1. Study Area

In this study three hospitals from Addis Ababa namely Tikur Anbessa Specialized Hospital SPHMMC, and Aabet Hospitals were selected due the following reasons Mentioned below. The study was conducted in the Tikur Anbessa Specialized Hospital (TASH), which is the largest public specialized hospital in Ethiopia and is affiliated with the Ethiopian Federal Ministry of Education (FMOE). The hospital has a capacity of 800 beds and is equipped with a team of 130 specialists and 50 non-teaching doctors. TASH provides diagnosis and treatment to approximately 370,000 to 400,000 patients every year, and its emergency department alone sees around 80,000 patients annually.

The study also conducted in Saint Paul hospital millennium medical college, Addis Ababa, which is second main government owned referral center. The college has more than 2,800 clinical, academic and administrative and support staff that provide medical specialty services to patients who are referred from all over the country, teaching medicine and nursing students and doing basic and applied researches. While the inpatient capacity is more than 700 beds, The College sees an average of 1,200 emergency and outpatient clients daily. Both hospitals are recognized for their expertise in treating neurological conditions, featuring both outpatient neurology departments and specialized services in the field.

AaBET Hospital is a part of St. Paul's Hospital Millennium Medical College. It is an emergency dedicated center. It provides emergency and critical care services, Orthopedic, Neuro-surgery, General surgery, and Plastics surgery services. The emergency department has 60 beds and the overall hospital bed is 300. Annual emergency room patient visits ranges from 15,000 to 20,000.

4.2. Study Period

From April to June 2023.

4.3. Study Design

Retrospective cross-sectional descriptive study; the medical records of all patients admitted with the diagnosis of seizure to the department of internal medicine, surgery and Emergency at SPHMMC, TASH and Aabet Hospital, from January 1, 2019 to September 30, 2022 were reviewed. The medical report of Statistics Office registered records of medical wards and ICU and registration books were reviewed to trace all cases.

4.4. Populations

4.4.1 Source Populations

All patients admitted with the diagnosis of seizure to the department of internal medicine, Surgery and Emergency of the three hospitals during the three-year period.

4.4.2 Study population

All patients admitted with the diagnosis of status epilepticus to the department of internal medicine, Surgery and Emergency of the three hospitals during the 3-year period and who full fill the inclusion criteria.

4.5. Inclusion and Exclusion criteria

4.5.1. Inclusion criteria

All patients fulfilling the definition of status epilepticus
Subjects included both sex who were >14years of age

4.5.2. Exclusion criteria

Those patients with incomplete recordings.

- Incomplete records- patients data records with no clear documentation of treatment provided and outcome.
-

4.6. Sample Size and Sampling Technique

All charts of patients admitted with the diagnosis of status epilepticus to the Department of Internal Medicine, Surgery and Emergency at SPHMMC, TASH and Aabet Hospital, from January 1, 2019 to September 30, 2022 were reviewed.

4.7. Study Variables

4.7.1. Dependent Variable

- Out comes status epilepticus
 - Improved
 - Deteriorated
 - Dead

4.7.2. Independent Variables

- Sociodemographic variables: age, gender, place of residence
- History of preexisting epilepsy
- Type of seizure
- Immediate likely cause of SE
- Serostatus of HIV/AIDS
- Complication(s) of SE
- Treatment provided

4.8. Operational Definitions

- **Status epilepticus:** a diagnosis of status epilepticus made by a physician, or when a patient's medical records indicate persistent seizure activity lasting for at least 5 minutes without interruption, or intermittent seizure activity where consciousness is not regained.
- **Etiology of SE [24]:**
 - Etiology was defined by the occurrence of a distant or recent symptomatic injury presumed to cause the episode.
 - Etiological factors were classified into categories such as medication discontinuation, cerebrovascular disorders, CNS infections, toxic-metabolic irregularities, trauma, neoplasms, and idiopathic.
 - Idiopathic etiology was assigned in the absence of conclusive clinical, laboratory, or radiological evidence substantiating a specific causative factor.
 - If clinical evaluation failed to reveal any identifiable cause, the SE was classified as idiopathic, even in cases where neuroimaging studies were not conducted on the patient.
- **Hypoxemia:** arterial oxygen saturation (SpO_2) of <90% by pulse oximetry.
- **Outcome at hospital discharge** recorded as
 - Improved -returned to baseline
 - Deteriorated - alive but substantially impaired relative to baseline clinical condition
 - Dead.
 - Good outcome includes improved patients.
 - **Poor outcome** included deteriorated and dead patients.

- **The cause of death** [24] was classified as either the primary underlying cause, SE itself along with its associated complications, or as unknown.

4.9. Data Collection Process and Quality Assurance

Data was collected from patient charts located in all medical ward, and intensive care units. It was collected by the investigator and data collectors using structured questioner. Data collectors were trained about the contents of the questionnaire and to collect the data in an accurate manner. Each paper was checked for completeness using format prepared by reviewing different literatures and undertaking modifications for the population studied. It was modified further after a pre-test. The data consisted demographic characteristics, history of preexisting epilepsy and use of antiepileptic drug (AED), type of seizure, immediate likely cause of SE, co-morbidities, complication(s) of SE, laboratory tests, brain imaging, treatment, outcome at hospital discharge, and cause of death. Data obtained from the study was coded and entered using the SPSS.

4.10. Data Processing and Analysis

Data was collected using self-prepared questionnaire and was checked manually for completeness. The information was extracted from patient charts. For data analysis SPSS version 26 was used. In the univariate analysis, age was assessed as a continuous variable, while pre-existing epilepsy, seizure type, etiology, and treatment were assessed as categorical factors. Continuous variables were analyzed using independent t-tests, while categorical variables were assessed using chi-squared tests. Multivariable logistic regression analysis was performed to determine associated factors of mortality. Odds ratios and significance levels were calculated along with 95% confidence intervals. The results presented using tables, graphs and pie chart. All tests with P-Value <0.05 were considered statistically significant.

4.11. Ethical Considerations

Ethical clearance was obtained from SPHMMC institutional review board and AAHB IRB. In addition, I asked internal medicine department head an informed consent on behalf of the patients for the charts that are reviewed. The confidentiality of the charts was kept and the information collected were used solely for the intended purposes. Identity and names were not included in the questionnaire and it was coded.

4.12. Dissemination of results

At the end of the research the findings will be distribute to the department of internal Medicine, neurology and ICU unit, health care providers and administrators of different

government hospitals. The results will be presented in SPHMMC and research symposium to give comment on what is currently known and the new findings that our study will provide underling the importance of evidence-based practice. This will provide possible directions on how to prevent or decrease the disease occurrence and will help to detect the patterns of the outcomes.

5. RESULTS

Sociodemographic characteristics

The study examined 224 patients diagnosed with Status Epilepticus (SE) across three healthcare institutions situated in Addis Ababa, specifically TASH, SPHMMC, and Aabet hospital. Of these patients, a slight majority were female (119; 53.3%), yielding a male-to-female ratio of approximately 1:1.14. The mean age of the participants was 37.81 years (± 15.22), with an age range spanning from 16 to 75 years. Notably, individuals falling within the age bracket of 20–39 years constituted the largest demographic subgroup, accounting for 117 cases (52.23%), while those aged under 20 years represented the lowest frequency with 18 cases (8.04%). Pre-existing epilepsy was documented in 77 patients (34.44%). Upon admission to the hospitals, the majority of patients (154, 68.89%) exhibited a Glasgow Coma Scale (GCS) score within the range of 9-14 out of 15. Eight-seven (38.9%) patients came from outside Addis Ababa. Eighty-three (37.05%) patients were admitted to the MICU. Further details regarding the sociodemographic and medical characteristics of the patients are provided in Figure 1 and Table 1.

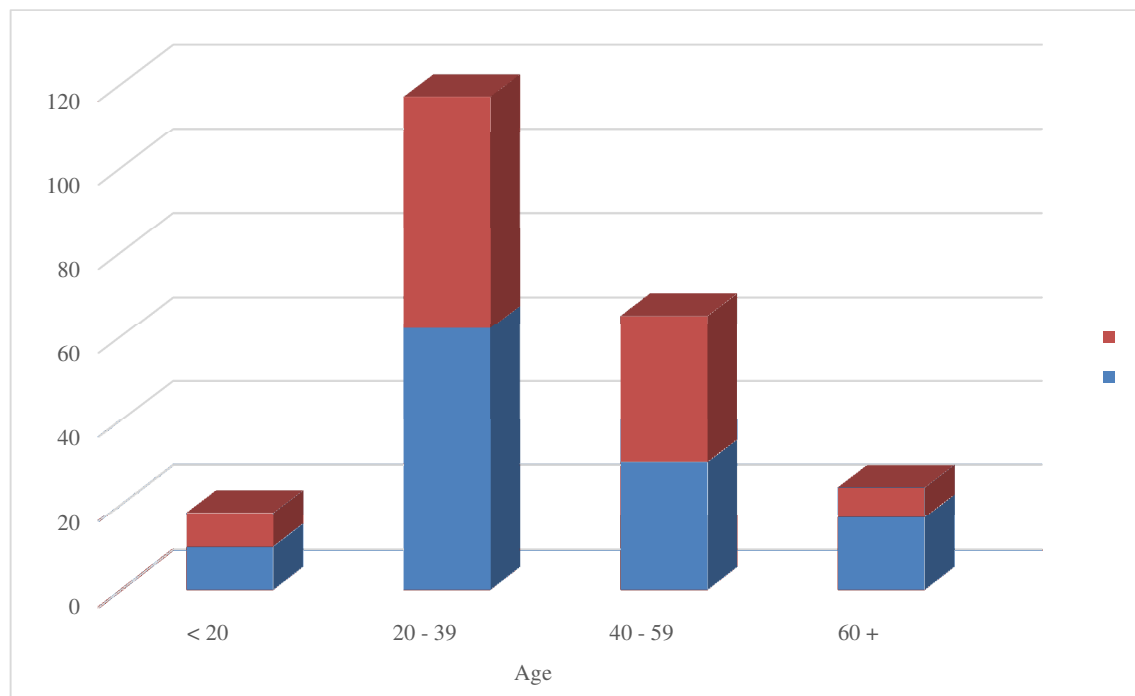


Figure 1: Age and sex distribution of patients with SE admitted to the selected hospitals.

Table 1: Socio demographic and medical characteristics of patients with SE admitted to the selected hospitals.

Variables		Frequency	Percent
Sex	Female	119	53.33
	Male	105	46.67
Age (yrs.)	< 20	18	8.04
	20 – 39	117	52.23
	40 – 59	65	29.02
	≥ 60	24	10.71
Place of residence	Addis Ababa	137	61.16
	Outside Addis Ababa	87	38.84
Place of admission	Emergency	90	40.18
	Ward	51	22.77
	ICU	83	37.05
Pre-existing epilepsy	No	145	64.44
	Yes	77	34.44
	Not documented	2	1.11
Seizure type	Primary generalized	177	78.89
	FWSG	42	18.89
	Not documented	5	2.22
GCS at initial presentation	9 - 14	154	68.89
	15	60	26.67
	<8	10	4.44
HIV/AIDS	Negative	174	77.78
	Unknown	40	17.78
	Positive	10	4.44

Etiology of SE

The primary etiologies contributing to Status Epilepticus (SE) were identified as follows: cerebrovascular accident (CVA) in 45 cases (20%), antiepileptic drug withdrawal (AEDW) in 40 cases (17.78%), central nervous system (CNS) infection in 30 cases (13.33%), and brain tumor in 27 cases (12.22%). CNS infections included meningitis (n = 18), brain abscess (n = 1), tuberculoma (n = 5), and toxoplasmosis (n = 2), with two cases of cryptococcal meningitis among meningitis patients. Lumbar puncture was performed in 73 patients (32.6%), revealing pleocytosis in 24 cases. Causative factors for SE are presented in figure 2.

The reasons identified for the discontinuation of AED were: no documented reason (n = 13), ran out of medication (n = 10), believed that he/she was “cured” (n = 7), and went to religious place (n = 10).

In patients with pre-existing epilepsy the commonest cause of SE was AEDW (40, 51.95%), while brain tumors and stroke accounting for 12 (15.6%) and 10 (13%) cases respectively. In patients with new onset seizure the commonest cause of SE was stroke (34, 23.45%), while CNS infection accounts for 27 cases (18.62%), both eclampsia and head trauma account for 17 cases (11.72%) each. Multiple possible etiologies for SE were identified in 10 (4.46%) patients, having two etiologies in all cases.

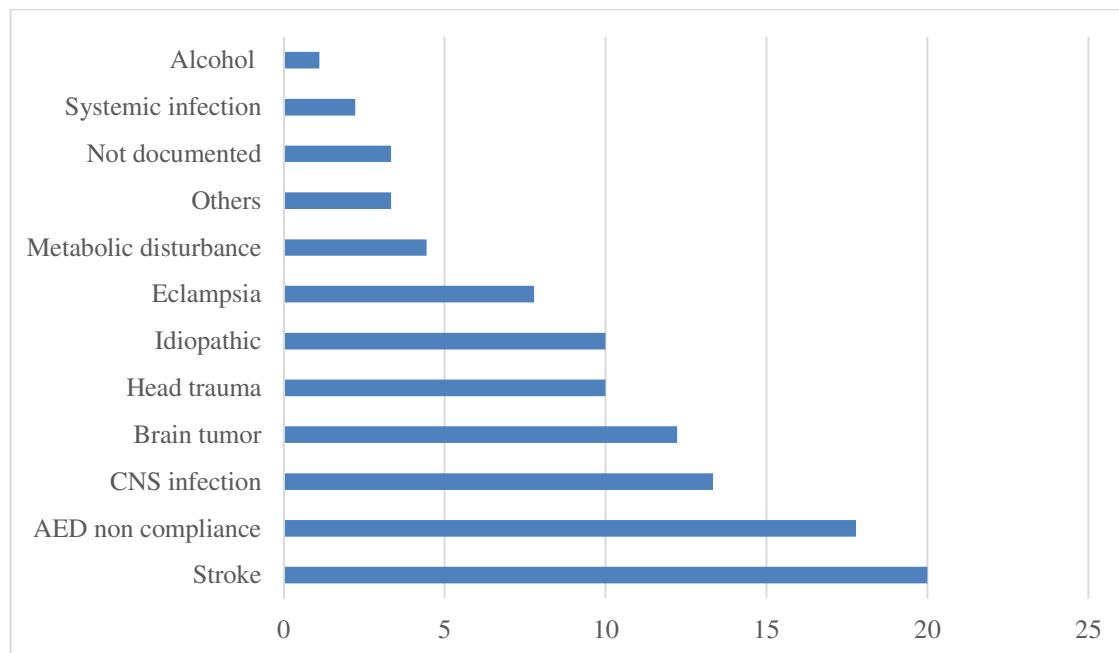


Figure 2: Etiologies of SE in patients admitted to the selected hospitals

Investigations

No electroencephalography (EEG) was conducted during episodes of Status Epilepticus (SE). Prior to current presentation, EEG was conducted in 27 patients (12.22%), revealing generalized epileptiform abnormalities in 5 patients, while 22 patients exhibited normal findings. Brain CT scans, either during or prior to SE onset, were performed in 92 cases (41.07%), identifying infarctions in 47 patients and hemorrhages in 22 cases (9.82%). Additionally, mass lesions (tumors or abscesses) were detected in 5 patients. MRI was conducted in 82 patients (36.6%), revealing mass lesions in 37 cases (16.5%). Normal MRI findings were observed in 30 patients (13.39%).

Complications

Complications of SE were observed in 117 cases (52.23%), with 60 cases (26.78%) experiencing two or more complications. Among patients without identified complications (n = 107) and those with only one complication (n = 55), there were no fatalities. However, among the 60 patients with multiple complications, 39 (65%) succumbed to their condition. The most prevalent complication, as detailed in Figure 3, was aspiration pneumonia, affecting 114 patients (51.11%). Hypoxemia and acute renal failure were observed in 55 cases (24.44%) and 17 cases (7.78%), respectively.

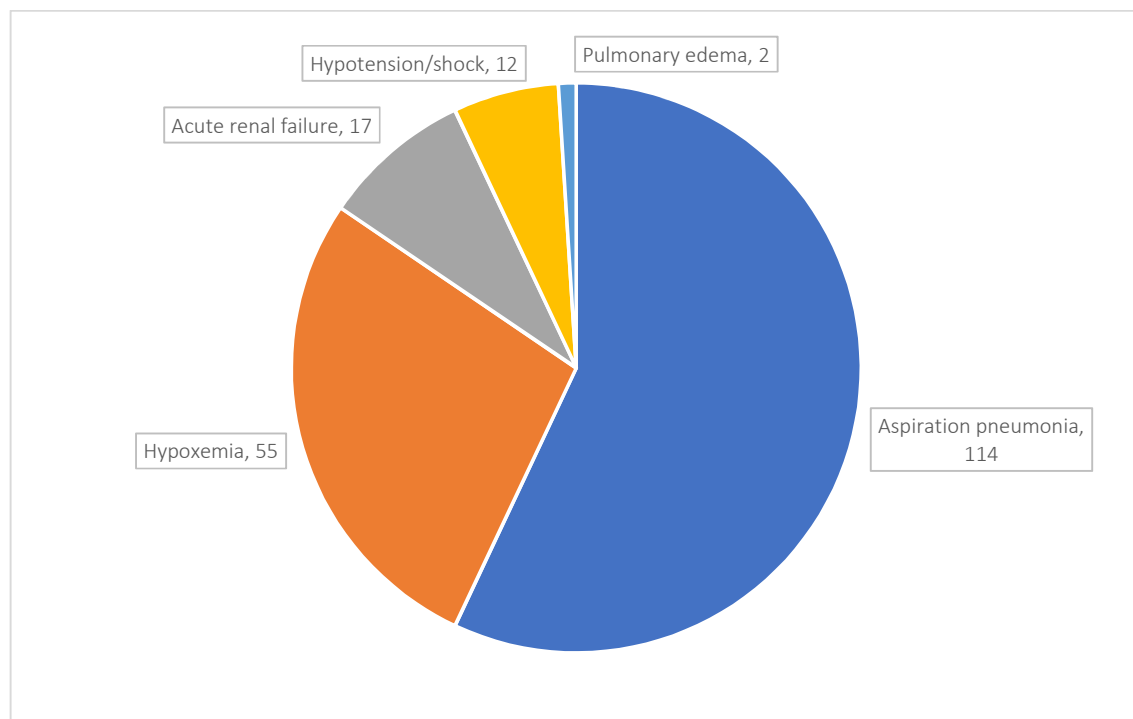


Figure 3: Complications in relation to outcome in SE patients admitted to the selected hospitals

Treatment

Prior to their presentation at the hospitals, 85 patients (37.78%) had received diazepam or another anticonvulsant. Following admission, 189 patients (84.37%) received intravenous (IV) diazepam, and 201 patients (89.73%) were administered oral phenytoin. Oral phenobarbital or carbamazepine was prescribed to 30 patients (13.33%) and 7 patients (11.8%), respectively. In 40 patients (17.86%), two or more antiepileptic drugs (AEDs) other than diazepam were utilized. General anesthesia was administered to 12 patients, while mechanical ventilation was required for 47 patients. The utilized options of treatments are displayed in the Table 2.

Table 2: Treatment options employed for patients with SE who were admitted to the selected hospitals.

Treatment given after admission	Frequency	Percentage
Phenytoin po	201	89.73
Diazepam	189	84.37
Antibiotics	112	50
Sodium valproate	50	22.22
Oxygen	50	22.22
Mechanical ventilation	47	21.11
Others	32	14.44
Phenobarbital	30	13.33
General anesthetics	12	5.56
Carbamazepine	7	3.33

Case fatality

In this study, a total of 39 fatalities were observed, accounting for 17.4% of the study population. Upon discharge, it was noted that 5 patients experienced a deterioration in their clinical condition, and subsequently opted for discharge against medical advice. Thus, 44 patients (19.64%), were identified as having poor outcomes. The primary cause of mortality was attributed to complications SE. Notably, a significant proportion of deaths (53.8%, n = 21) occurred within the age range of 20–39 years.

CNS infection emerged as the predominant etiology of status epilepticus (SE) among deceased patients (18 cases), followed by stroke (9 cases) and head trauma (2 cases).

Multivariable logistic regression analysis, which is shown in Table 3, indicated that factors significantly linked to mortality in patients with SE include HIV/AIDS with its central nervous system (CNS) complications, CNS infection, and the presence of two or more complications.

Table 3: Multivariable analysis to determine factors associated to mortality in patients with SE who were admitted to the selected hospitals.

		dead n. (%)	p-value	AOR (IC 95%)
Age Group	20 - 39 years	19	ref	Ref
	40-59 years	13	0.129	0.76 (0.13–4.19)
	60 + years	7	0.885	1.37 (0.99 – 2.51)
Sex	Female	26	0.914	3.94 (0.40–19.32)
	Males	13	Ref	Ref
Preexisting epilepsy	No	26	Ref	Ref
	Not documented	6	0.326	1.79 (0.13–3.69)
	Yes	7	0.342	0.83 (0.19–7.19)
HIV AIDS	Negative	28	0.527	0.74 (0.43–4.43)
	Unknown	6	Ref	Ref
	Positive	5	0.046	3.50 (0.97–18.75)
Etiology	Stroke	9	0.155	2.22 (0.31–13.84)
	AED non compliance	1	0.264	1.40 (0.38–5.97)
	CNS infection	18	0.034	4.61 (0.99–21.33)
	Brain tumor	1	0.113	0.97 (0.10–9.51)
	Head trauma	2	0.212	2.22 (0.35–13.84)
	Idiopathic	1	Ref	Ref
	Eclampsia	2	0.077	0.62 (0.36–2.81)
	Metabolic disturbance	1	0.387	0.93 (0.42–3.11)
	Others	2	0.224	1.29 (0.08–7.51)
	Not documented	1	0.753	1.14 (0.13–2.19)
	Systemic infection	1	0.192	2.76 (0.13–3.19)
	Alcohol	1	0.426	1.25 (0.13–5.19)
Complications	Two or more	39	0.002	10.50 (1.44–76.28)

6. DISCUSSION

Our study aimed to assess various aspects of status epilepticus (SE) in patients at the largest three referral hospitals in Ethiopia, including clinical presentation, causes, complications, treatment, outcome, and associated factors with mortality. In this study, SE was more prevalent among females (53.33%), this is in agreement with Lisa Langenbruch et al study, which found that female sex is associated with a history of SE. [34]

The mean and median ages of patients were 37.8 and 35 years, respectively. This comparable with Amanuel et al. study in Ethiopia, where the median age was 36 years [24]. But it is different from the mean age of around 50 years, in a study from Cameroon, and Thailand [35] [36]. A study by M.P. Malter et al finding in which older patients represented the predominant subgroup in patients with SE; this difference might be explained by the fact that older patients suffered more often from non-convulsive semiology than younger patients. [37]

In this study pre-existing epilepsy was found in 77 patients (34.44%). This finding is similar with the previous studies, in which about 40% of patients with SE have a history of epilepsy. [38] The most common documented SE seizure type in our study was primarily generalized (78.89%), followed by FWSG (18.89%). This is different from a study by László Horváth et al, in which focal, generalized and combined type epilepsies account for 49.6%, 34.8%, and 15.6% of SE, respectively. [26] However, in Nigeria, proportions comparable to ours were found (71.1% primarily generalized, 11.8% FWSG, and 17.1% simple partial). [39] This is also comparable with previous Ethiopian study, primarily generalized (60.5%), followed by FWSG (36%) and simple partial (3.4%). [24]

Nonconvulsive SE was not identified in our study. Because patients with NCSE can exhibit a wide variety of clinical features ranging from coma, confusion, speech disturbance, aphasia, autonomic manifestation, delusions, to behavioral manifestations, including hallucinations, and paranoia, a high index of suspicion is often required and the distinction often rests on electroencephalography (EEG) finding. [39]

The etiological spectrum of SE in the current study was in agreement with what was reported from other developing countries study. The most common causes of SE in our study were stroke (20%), AEDW (17.78%), CNS infection (13.33%), followed by brain tumor (12.22%). In Nigerian study, stroke was the most common etiology (28.9%), followed by AED noncompliance (21.1%), CNS infections (19.8%), metabolic causes (15.7%), and CNS tumor (9.2%). [39] In contrast to previous study done in TAH, in which CNS infection (36%) was

the most common cause of SE, followed by AEDW (17.6%) and idiopathic (16.8). [24] This temporal change of etiologies might be explained by rising incidence and prevalence of NCDs in Ethiopia [40], as well as According to Adeloye, the burden of stroke in Africa is high and still increasing. [41]

Poor compliance with antiepileptic drug resulting in exacerbation of a pre-existing seizure disorder is the second most common cause (17.78%) in this study. In Ethiopian and Nigerian hospital-based studies, AEDW was a cause of SE in 17.6% and 21.1% respectively. [24, 39] This finding, which is in keeping with other reports, deserves further elaboration as it is a preventable precipitant of SE. Previous studies have shown that poor adherence to AED is associated with a three-fold higher risk of dying. [42, 43]

The study found that infection with HIV/AIDS and its associated CNS complications were significantly associated with mortality in patients with status epilepticus (SE). This finding was similar with that of previous study in Ethiopia, in which SE in patients with concurrent HIV infection had 6.7 OR of mortality [24], and study in USA also showed the in-hospital mortality was significantly higher in status epilepticus patients with underlying HIV infection [44].

CNS infection was the third common cause of SE in our study (13%). This is in agreement with a study from Cameroon and Nigeria, where CNS infection accounts for 16.9% and 19.8% SE respectively. [35, 39] In contrast to our findings, previous Ethiopian study showed that CNS infection was cause for SE in 36%. [24] This decreased proportionality of CNS infection is due to the increased incidence of NCD and strokes in Ethiopia other African counties. [40, 41]

Prior to hospital admission, 37.78% of patients had received anticonvulsant therapy. Aligning with these findings, a Canadian study noted that 46% of patients presenting with status epilepticus were prescribed antiepileptic drugs prior to admission.[45] This percentage exceeded the reported preadmission treatment rate of 17% in a study conducted in Italy [9], while falling below the 59% observed in another study. [7] Notably, our analysis revealed no statistically significant difference in case fatality rates between patients treated with anticonvulsants before hospital arrival and those who were not.

The in-hospital case mortality rate observed in this study was 17.4%, which aligns with the findings reported by Amanuel et al. (20.2%) [24]consistent with the general trend observed across various studies conducted in both developed and developing nations. Lower mortality

rates were reported by Knake et al. (9.4%) in Germany [2] and by Coeytaux et al. (7.6%) in Switzerland [7].

However, Vignatelli et al. documented a higher mortality rate of 39% [9]. In Africa, the range of in-hospital case mortality varies between 16.9% and 24.8%, with variations noted based on the age of the patients. [35, 39, 46]

This study has several limitations that warrant careful interpretation of the findings. There was no EEG availability to confirm status epilepticus diagnosis and classification, relying only on clinical documentation which can be inaccurate. Details on precise seizure onset time, timing of treatment initiation, specifics of interventions administered and duration of time required to control the seizure were often poorly documented or missing, limiting capture of critical data like treatment lags. Additionally, incomplete or ambiguous information was common due to retrospective reliance on existing medical records and inconsistent documentation practices. Key parameters may have been omitted. Finally, as a retrospective investigation, this study was constrained by the quality and completeness of records available. Overall, these limitations highlight the need for improved access to diagnostic modalities, standardized documentation procedures, precise timekeeping during acute presentations, structured data gathering, and large-scale prospective studies to substantiate the findings. However, this study provides a useful preliminary overview of status epilepticus profiles and outcomes in this clinical setting.

7. CONCLUSIONS

The mean age of patients was 37.8 years, with a slight female predominance. Stroke (20%), antiepileptic drug withdrawal (17.8%), central nervous system infections (13.3%), and brain tumors (12.2%) were the leading etiologies of SE. This study found a concerning high complication rate of over 50%, mainly aspiration pneumonia and case fatality rate of 17.4% among SE patients, underscoring the need for better prevention and management protocols. With stroke emerging as the leading cause, the findings underscore the growing burden of non-communicable diseases, while preventable factors such as infections and treatment non-compliance continue to substantially contribute to SE incidence. Patients with multiple complications, CNS infections, or HIV/AIDS co-morbidities had significantly higher mortality rates, emphasizing the importance of targeted interventions in these high-risk groups

8. RECOMMENDATIONS

- Further studies should be conducted to better characterize SE semiology, with a focus on identifying non-convulsive status epilepticus
- Include EEG confirmation and detailed documentation of seizure onset/duration and treatment timelines to accurately classify cases
- Implement guideline-based protocols for early treatment and prevention of status epilepticus complications.
- Public awareness campaigns are needed to improve medication compliance among epilepsy patients to prevent SE secondary to AED withdrawal
- Targeted interventions should focus on reducing modifiable risk factors like HIV/AIDS, CNS infections, and complications to improve SE outcomes

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ANNEXES

1. INFORMATION LIST

RESEARCH TITLE:

CLINICAL CHARACTERISTICS, OUTCOME, AND FACTORS ASSOCIATED
WITH MORTALITY IN PATIENTS WITH STATUS EPILEPTICUS AT
SELECTED PUBLIC HEALTH HOSPITALS IN ADDIS ABABA, ETHIOPIA

PRINCIPAL INVESTIGATOR:

Dr Mihiret Legese (Internal Medicine Resident)

Phone number: 251974078915

Email address: mihiretlegese25@gmail.com

ADVISORS:

Dr Tesfaye Berhe (consultant internist, Neurologist)

Mrs. Sisay Tanie (MSc, Biostatistician)

SPONSOR:

St. Paul's Hospital Millennium Medical Collage

2. QUESTIONNAIRE

Data collection tools/questionnaire

I: Socio-demographic status

S. Number	
1.1 Card number	
1.2 Questioner number	
Sex	A. Male
	B. Female
Age	
Place of residence	A. Addis Ababa
	B. Outside of Addis Ababa

II: Clinical characteristics of patients

Variable	
Preexisting epilepsy	A. Yes
	B. No
	C. Not documented
Seizure type	A. Simple partial
	B. FWSG
	C. Primary generalized
	D. Not documented
GCS at initial presentation	A. <8
	B. 9-14
	C. 15
	D. Unknown
Place of admission	A. Emergency
	B. Ward
	C. ICU
HIV/AIDS	A. Positive
	B. Negative
	C. Unknown
Etiology	A. CNS infection
	B. AED non compliance
	C. Idiopathic
	D. Metabolic disturbance
	E. Stroke
	F. Brain tumor
	G. Systemic infection
	H. Head trauma
	I. Alcohol
	J. Eclampsia
	K. Other
	L. Not documented

III. Neuroimaging/EEG, laboratory Findings Treatment and Prognosis of Patients.

Brain CT finding	A. Mass
	B. Infraction
	C. Hemorrhage
	D. Normal
	E. Not documented
Brain MRI finding	A. Mass
	B. Infarction
	C. Hemorrhage
	D. Normal
	E. Not documented
Was LP done?	A. Yes
	B. No
If yes	A. WBC
	B. Protein
	C. Glucose
	D. Gram stain
	E. Other tests
Previous EEG	C. Generalized
	D. Focal
	E. Normal
	F. Not documented
EEG done during current presentation	A. Generalized
	B. Focal
	C. Normal
	D. Not documented
Treatment given at referral	A. Antiepileptic
	B. Others
	C. Not documented
	D. None
Treatment given after admission	A. AEDs
	a. Phenytoin po
	b. Phenytoin IV
	c. Diazepam
	d. Phenobarbital
	e. sodium valproate
	f. carbamazepine
	B. General anesthetics
	C. Antibiotics
	D. Oxygen
	E. Mechanical ventilation
	F. Others

IV. Complications and outcome

Complication	A. None
	B. Aspiration pneumonia
	C. Hypoxemia (Sao2 < 90%)
	D. Hypotension/shock
	E. Acute renal failure
	F. Pulmonary edema
	G. Cardiac arrhythmia
	H. Orthopedic injury
	I. Rhabdomyolysis
	J. Others
	K. Not documented
Outcome	A. Improved
	B. Deteriorated
	C. Dead
If dead, cause of death	A. Primary underlying cause
	B. SE itself along with its associated complications
	C. Unknown

3. ASSURANCE OF INVESTIGATOR

I the undersigned resident agree to accept all responsibilities for the scientific, ethical and technical conduct of the research project and for provision of required progress reports as per terms and conditions of the Research and Publication Directorate and /or Department of Public Health of St. Paul's Hospital Millennium Medical College.

Name of the Resident: Dr Mihiret Legese

Signature: _____

Date: _____

Approval of Advisors:

Name of Public Health Advisor: Mrs. SisayTanie (MSc, Biostatistician)

Signature: _____

Date: _____

Name of clinical advisor: Dr Tesfaye Berhe (MD, Neurologist)

Signature: _____

Date: _____