EVALUATION OF BENEFICIAL EFFECTS OF LEVETIRACETAM AND CARBAMAZEPINE IN POST STROKE EPILEPSY

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CERTIFICATION

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DEDICATION

This work is dedicated to all patients suffering from stroke and epilepsy.

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ABSTRACT

Post-stroke Epilepsy (PSE) has been identified as a significant clinical condition in stroke survivors affecting outcome, quality of life, and hospital cost. They are clinically underestimated without consensus for prophylaxis and treatment. The PSE were empirically managed with older Anti-Epileptic Drugs (AEDs) like Carbamazepine (CBZ), which is not without issues on side effect, drug-drug interactions, and tolerability. Newer AEDs like levetiracetam (LEV) have better safety and tolerability profiles, however there is limited clinical evidence supporting its use in the treatment and prevention of PSE. This study was therefore designed to identify determinants of PSE and compare prophylactic and therapeutic effects of LEV and CBZ monotherapy.

The study was divided into three phases and carried out in three purposively selected tertiary health institutions in South West Nigeria. The first phase involved detailed review of records for socio-demographics, aetiology and medication characteristics of 946 adults, aged ≥16, and attending epilepsy clinics for a minimum period of 5 years using convenient sampling method. In the second phase, 346 neuroimage confirmed stroke patients who consented were recruited and followed up for 24 months. Post Stroke Outcome (PSO) such as severity, functional outcome, cognition and epileptiform pattern were assessed using National Institute of Health Stroke Scale (NIHSS), Modified Ranking Scale (MRS), Cognitive Screening Instrument for Dementia (CSID), and Electroencephalography (EEG), respectively. Development of PSE, Mortality Rate (MR) and determinants of PSE were evaluated. Those that developed seizures were randomised into AED groups and followed up for 12 months and PSO evaluated. The third phase recruited 240 neuroimage confirmed stroke patients with no prior seizure history and randomly divided into Prophylactic Group (PG) [80 each of LEV and CBZ] and Non-Prophylactic Group (NPG). The Lev (250mg) and CBZ (200mg) were administered twice daily and evaluated for PSO. Data were analysed using descriptive statistics, Chi square, and independent student's t test at $\alpha_{0.05}$.

The records showed that majority of the patients had idiopathic (60.1%) and structural epilepsy (24.9%), with stroke being the commonest. Two hundred and ninety-four 294(31.1%) were not on AED and 515(79.0%) of those on AEDs used CBZ. Twenty-seven percent (27%) developed PSE and identified determinants of PSE were severe stroke (p0.010), diabetes mellitus (p0.002), cortical involvement (p0.016), insomnia (p0.009) and epileptiform pattern (p0.000). Comparing CBZ with LEV groups among PSE, PSO showed higher MR [21(45.7%) versus 11(23.9%), p0.029], poor outcome on MRS [28(63.6%) versus 17(40.5%), p0.032], severe NIHSS [26(56.5%) versus 13(28.3%), p0.006] and impaired cognition on CSID [20(43.5%) versus 16(34.8%), p0.08], respectively. In phase 3, 17(10.6%) of PG [10(12.8%) CBZ versus LEV 7(8.8%)] compared to 17(21.3%) of NPG developed seizures. There was higher MR [22(13.7%) versus 34(42.5%), p0.029], poor outcome on MRS [(47(58.8%) versus 59(36.9%), p0.001)], and CSID score (53.39±26.19 versus 36.37±34.06,

p0.001) in NPG compared with PG.

Stroke severity, cortical involvement, epileptiform pattern and background diabetes mellitus were identified as predictors of post stroke epilepsy. Levetiracetam exhibited better therapeutic effect than carbamazepine for prophylaxis and treatment of post stroke epilepsy.

Keywords: Anti-Epileptic Drugs, Stroke, Seizure, Prophylaxis
Word count: 484

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MHD- 10-monohydroxy metabolite

ADC-Apparent Diffusion Coefficient

ACA- Anterior Cerebral Artery

AEDs- Anti-Epileptic Drugs

AEDP- Anti – Epileptic Drug Prophylaxis

BI- Barthel Index

BBB- Blood Brain Barrier

CBZ- Carbamazepine

CBF- Cerebral Blood Flow

CBV- Cerebral Blood Volume

CSID- Cognitive Screening Instrument for Dementia

CT- Computed Tomography

CI- Confidence Interval

CEMRA- Contrast Enhanced

CAVE- Cortical location, younger Age, Volume of hematoma and acute symptomatic seizure

CSD- Cortical Spreading Depolarization

CA1- Cornus Ammonis 1

CA3- Cornus Ammonis 3

CFR- Case Fartality Rate

CTA- CT Angiography

CTP- CT perfusion

DBP- Diastolic Blood Pressure

DWI- Diffusion-Weighted Imaging

EEG- Electroencephalogram

FBG- Fasting Blood Glucose

FMCA- Federal Medical Centre, Abeokuta

FLAIR- Fluid-Attenuated Inversion Recovery

GABA- Gamma Aminobutyric Acid

GOS- Glasgow Outcome Scale

GBD- Global Burden of Disease

HbA1c- Glycated Haemoglobin

GRSW- Gradient –Recalled Susceptibility-Weighed

HMG- Haemorrhagic Patients

HSPWS- Haemorrhagic Stroke Patients with Seizures

HDL- High-Density Lipoprotein

HU- Hounsfield unit

ICP- Intracranial Pressure

ISCH- Ischaemic Patients

ISPWS- Ischaemic Stroke Patients with Seizures

LACI- Lacunar Infarcts

LEV- Levetiracetam

LDL- Low-Density Lipoprotein

MRI- Magnetic Resonance Imaging

mTORC1- Mammalian Target of Rapamycin Complex 1

MCA- Middle Cerebral Artery

MRS- Modified Rankin Scale

MR- Mortality Rate

MRA- MR Angiography

MRP- MR Perfusion Imaging

NCEP- National Cholesterol Education Program

NIHSS- National Institute of Health Stroke Scale Score

NLC – National Population Commission

NMDA- N-Methyl-D-aspartate

NAEDP- No Anti – Epileptic Drug Prophylaxis

NSIE- Non-Stroke Induced Epilepsy

OOUTH- Olabisi Onabanjo University Teaching Hospital

OR- Odd Ratio

OXC- Oxcarbazepine

OCSP- Oxfordshire Community Stroke Project

PACI- Partial Anterior Circulation Infarcts

PWI- Perfusion-Weighted MRI

PAR- Population Adjusted Risk

PCA- Posterior Cerebral Artery

POCI- Posterior Circulation Infarcts

PSS- Post Stroke Seizures

PSE- Post-stroke epilepsy

PoSERS- Post-Stroke Epilepsy Risk Scale

PRoFESS- Prevention Regimen for Effectively Avoiding Second Strokes

PTE- Pulmonary Thromboembolism

ROS- Reactive Oxygen Species

SPS3- Secondary Prevention of Small Sub-Cortical Stroke

SD- Standard Deviation

SIE- Stroke-Induced Epilepsy

SPARCL- Stroke Prevention by Aggressive Reduction of Cholesterol Levels

SSA- Sub-Saharan Africa

SV2A- Synaptic Vesicle Protein 2A

SBP- Systolic Blood Pressure

ATP-III- The Adult Treatment Panel

ILAE- The International League Against Epilepsy

TACI- Total Anterior Circulation Infarcts

TOAST- Trial of ORG 10172 In Acute Stroke Treatment

UCH- University College Hospital

VLDL- Very Low-Density Lipoprotein

WHO- World Health Organization

CHAPTER ONE
INTRODUCTION

1.1: Background

Stroke is the third leading cause of death and a major cause of disability in developed countries, affecting one in six adults, with an estimated 3–6 million cases annually (Lahti *et al.,* 2017). A previous retrospective study, that spanned over ten years, involving case notes and autopsy records, among stroke patients in Southwestern Nigeria, that were diagnosed based on World Health Organization (WHO) criteria reveal that stroke accounts for about 2% cause of death rate and a Case Fatality Rate (CFR) of about 10% at 24hours, 30% at 7days, and greater than 40% at 30days and 6month (Ogun *et al*., 2005) In a cohort of 603 consecutive stroke patients, 59% had complications and were mostly common in elderly. Recurrent falls, fracture, depression, cognitive impairment, urinary tract and chest infection, deep venous thrombosis, pulmonary embolism, acute confusional state, and epilepsy are known sequelae of stroke (Fantu *et al*., 2022; Farooq and Gorelick, 2013; Kodankandath *et al*., 2017)

Stroke Induced Seizures (SIS) are associated with prolonged hospitalization, more complications and increased mortality especially in elderly. While Stroke Induced Epilepsy (SIE) is a major clinical condition among stroke cohort affecting outcome, quality of life, and cost of hospital care (Doria and Forgacs, 2019) . The International League Against Epilepsy (ILAE) defined SIE as two or more unprovoked epileptic seizures occurring at least a week after stroke (Brodie *et al*., 2018). Seizure Induced Seizure are further subdivided into early onset and late-onset seizures based on time of occurrence. According to the present ILAE definition, a single late seizure after stroke qualifies as structural epilepsy due to the high (>60%) risk of recurrence within the following 10 years (Fisher, 2017).

Stroke is the leading cause of epilepsy in the elderly population, accounting for nearly 50% of the newly diagnosed cases of epilepsy in this age group *(*Zhao *et al.,* 2018*).* In a meta-analysis of 34 longitudinal cohort studies involving 102,008 patients, the aggregate incidence rate of SIS is 7% while that of SIE was 5% (Zou *et al*., 2015a)

In another study using WHO criteria for stroke diagnosis and physician supervised questionnaire-based diagnosis of epilepsy study to describe epidemiology and association of SIE, among 3,310 patients with no prior history of epilepsy who presented with first stroke between 1995 and 2007, with a mean follow-up of 3.8 years. Two-hundred thirteen subjects (6.4%) developed SIE. SIE incidence at 3 months and 1, 5, and 10 years were estimated at 1.5%, 3.5%, 9.0%, and 12.4%, respectively (Graham *et al*., 2013a) Gender and demographic factors were not associated, however, univariate analysis revealed association with cortical involvement, young age and stroke severity at presentation Kammersgaard and Olsen. reported from a community study that SIE occurred in about 3% of all patients with stroke within 7 years after stroke (Kammersgaard and Olsen, 2005) Generally, the incidence of SIE in older people ranges from 2% to 4% (Graham *et al*., 2013b).

Bentes and colleagues reported that SIE is clinically underdiagnosed without adequate neurophysiological assessment (Bentes *et al*., 2017) Bentes and colleagues observed that independent predictors of SIE are asymmetry and interictal epileptiform pattern.

Epileptogenesis is defined as a molecular and cellular process of converting a less susceptible brain to one that is highly excitable leading to recurrent seizures (Webster *et al*., 2017; Yang *et al.,* 2018) The exact pathogenic mechanism of SIE has not been elucidated, however, recent observations suggests inflammation may play a role leading to molecular reorganization of membrane and extramembrane proteins, neuronal loss, gliosis, axonal dendritic and mossy sprouting (Rana and Musto, 2018).

Generally, epilepsy is due to an imbalance between activities of excitatory and

inhibitory neurotransmitters (Yang *et al.*, 2018) Paroxysmal depolarization shift is defined as burst of aggregation of consistent discharges which is in form of protracted action potential. It is key to investigating epileptogenic focus and indeed a reliable marker of epileptogenesis (Zöllner *et al.,* 2021).

1.2: Rationale

Consequent upon the scant knowledge of the pathogenesis of SIE, its management remains largely empirical. There is also no consensus for primary prevention of SIE (Winstein *et al.,* 2016). Anti-Epileptic Drugs (AEDs) such as Carbamazepine (CBZ), Phenytoin, and Sodium Valproate are employed in the treatment of SIE and SIS. Recently, newer AEDs for example, Levetiracetam (LEV), an anti-epileptic with a unique mode of action, was introduced into the management of SIE.(Litvinova *et al.*, 2020; Shetty, 2013a) There are growing evidences supporting the role of LEV in the management of SIE. Levetiracetam has been described to inhibit inflammatory activities and gliotic changes that can induce seizures in hippocampus and piriform cortex of rat (Lyseng-Williamson, 2011). Seizure Induced Epilepsy, is one of the key sequelae of stroke with potential serious consequences and requires adequate clinical management to reduce associated morbidity and mortality. Management of SIE has not attracted the deserved attention in Nigeria. Therefore, there is urgent need to evaluate the potential impact of AED in prophylaxis and management of SIE in Nigeria. The study was conducted in three phases with a view to improving outcome of stroke particularly in the management of epilepsy secondary to stroke.

1. Hospital-based pattern of epilepsy among adults (and adolescents) Nigerians in South western Nigeria
2. Pattern of seizure disorder and evaluation of LEV and CBZ in the management of SIS/SIE among stroke survivor.
3. Evaluation of the role of Levetiracetam and Carbamazepine in the prevention of SIS.

1.3: Aim of Study

To identify determinants of Post Stroke Epilepsy (PSE) and compare prophylactic and therapeutic effects of Levetiracetam (LEV) and Carbamazepine (CBZ) monotherapy

1.4: Specific Objectives

1. To determine hospital-based pattern of epilepsy among the adult (and adolescents) population attending selected epilepsy clinics in Southwest, Nigeria.
2. To determine pattern and clinical predictors of Stroke-Induced Seizure (SIS)/Stroke-Induced Epilepsy (SIE) among stroke survivors.
3. To compare efficacy and tolerability of Levetiracetam (LEV) and Carbamazepine (CBZ) in stroke-induced epilepsy.
4. To determine the prophylactic role of Levetiracetam (LEV) and Carbamazepine (CBZ) in stroke-induced seizure (SIS)/stroke-induced epilepsy (SIE).

1.5: RESEARCH QUESTIONS

1. Is there a need for AED as prophylaxis among stroke patients?
2. Which of the selected AED will exhibit better prophylactic and therapeutic efficacy?
3. What are the clinical predictors of PSE?
4. Does stroke and PSE affect cognitive outcome?
5. Does the type of AED used affect the cognitive outcome?

CHAPTER TWO
LITERTURE REVIEW

2.1: Burden of stroke

Stroke is an important of cause of disability, seizures, cognitive impairment and mortality in adults worldwide (Akinyemi, *et al.*, 2021). It is estimated that an average of 1 in 4 individual that are adult will likely develop stroke in his/her lifetime (Akpalu *et al.*, 2019). The burden of stroke is rising in sub-Saharan Africa (SSA) compared to data from developed countries, though overall indices are worse in developed countries with current prevalence of 1.1 per 1000 and a month fatality rate of about 40% (Akpalu *et al.*, 2019). The increasing mortality of stroke from SSA has been linked to suboptimal and non -availability of adequate stroke care compared to what obtains in the developed countries (Onwuchekwa *et al.*, 2014).

Identified key drivers of increasing stroke burden has been classified into early, adolescent, and adult factors according to a recent view by *Akinyemi* et al. The factors that are related to early life issues include low birth weight and childhood under nutrition (Akinyemi *et al.*, 2021). Specifically low birth weight has been linked to a lot of cardiovascular risk including hypertension, dyslipidaemia and diabetes in late life (Akinyemi *et al.*, 2021). The adolescent and young adulthood factors were related to lifestyle modification and social changes including excessive intake of alcohol and meat, smoking, and reduced intake of vegetables (Olowoyo *et al.*, 2021). Also from adolescent to adulthood, air pollution and epigenetic factors from stress further aggravate neurological diseases by promoting inflammatory cascade (Akinyemi *et al.*, 2021). Previous studies on stroke review that the incidence of stroke ranges from 26/100000 to 61/100000 (Adeloye 2014; Ezejimofor *et al.*, 2017). The incidence of stroke is higher in male compared to female before menopause, however, the risk is equal after menopause (Akpalu *et al.,* 2019). The current estimated prevalence of stroke ranges from 56/100000 to 316/100000 per 100,000 in SSA.

Worldwide, there has been 3.1% rise in age standardized stroke prevalence rate (1300.6 UI, 1229.0-13747 per 100000 in 2017) (Kim *et al.*, 2020). Stroke mortality rate in Nigeria is high with a reported 30-day CFR < 40%. The CFR is about 8times higher in the developing nation compared to developed countries. There has been 34% decrease in age standardized stroke mortality rate worldwide (Obiako *et al.*, 2011).

2.2: Risk factors

Stroke risk factors can be divided into two categories, modifiable and non-modifiable, with age being one of the most important non-modifiable risk factors (O'Donnell et al., 2010, 2016). A recent study defining the main modifiable risk factors for stroke in cohorts from Ghana and Nigeria found hypertension, dyslipidaemia, regular meat intake, and increased waist-to-hip ratio, diabetes, low intake of green and yellow vegetables, stress, too much salt at the table, heart disease, lack of exercise, etc. Current smoking is an identified modifiable risk factor (Akpalu *et al.*, 2019; Azarpazhooh et al., 2019). An international study of stroke risk factors found that majority of strokes are caused by 20 risk factors. These factors include hypertension, Diabetes Mellitus (DM), heart related problems, active smoking, and central obesity, dyslipidaemia, lack of exercise, alcohol intake, poor diet habit, psychosocial stress, and depression (Guzik and Bushnell, 2017; O'Donnell *et al.*, 2016).

Consistently, hypertension is one of the leading factor contributing to development of stroke worldwide from previous study as described by the INTERSTROKE study (O'Donnell et al., 2010, 2016). Studies have shown that variability in Blood Pressure (BP), isolated rise in Systolic BP (SBP), Uncontrolled Diastolic BP (DBP), concomitant rise in SBP and DBP were all associated with stroke, severity, and poor outcome (Guzik and Bushnell, 2017; Prabhakaran and Chong, 2014). The target aim of BP control should be a decline of 10-mmHg and 5-mmHg in SBP and DBP, respectively from baseline in hypertensive, non-hypertensive, DM and Chronic Kidney Disease (CKD) patients (Guzik and Bushnell, 2017; Hajjar *et al.*, 2010; Leasure *et al.*, 2019).
Data from Secondary Prevention of Small Sub-Cortical Stroke (SPS3) and

Prevention Regimen For Effectively Avoiding Second Strokes (PRoFESS) suggest that SBP should be between 120 to 140 mmHg and DBP should be between 80 to 90 mmHg to decrease re-occurrence of Stroke (Diener, 2007). There are now changes in previous targets from guidelines which is recommending commencement of BP medication at a higher value for adult aged >60years specifically at >150/90mmHg. Furthermore, recent guidelines are recommending value of 140/90 in DM and CKD patients (AlAhmad *et al.*, 2021).

Diabetes Mellitus, and impaired fasting glucose are major risk factor for ischemic stroke from previous study (Chen *et al.*, 2016). Diabetes Mellitus accelerates the process of atherosclerosis in people with dyslipidaemia, high BP, and obesity (Chen *et al.*, 2016). Exercise, diet intervention, Oral Hypoglycaemic Agents (OHA) and/or insulin aimed at tight glycaemic control with glycated haemoglobin <7 are beneficial in stroke prevention (Akpalu et al., 2019; Chen et al., 2016). Dyslipidaemia is another significant risk factor for stroke. Data available from several studies indicate that low-density lipoprotein (LDL) and Very-Low-Density Lipoprotein (VLDL) levels are associated with ischemic stroke, whereas High-Density Lipoprotein cholesterol (HDL)and triglyceride levels are indicated that it did not (Guzik and Bushnell, 2017; Hackam and Hegele, 2019; Kim *et al.,* 2020). Lowering LDL cholesterol levels is a major goal of post-stroke dyslipidaemia treatment, primarily through the use of statins (Guo *et al.*, 2015; Hackam and Hegele, 2019; J. Kim *et al.*, 2020). Furthermore, statin use in primary or secondary stroke prevention is associated with a 21% reduction in stroke risk per mmol (or about 39 mg/dl) has been associated with lower LDL cholesterol levels. The recent guidelines suggest a strict 50% reduction in LDL levels, or absolute levels below 70 mg/dl. The SPARCL study (Stroke Prevention by Actively Lowering Cholesterol Levels), the Adult Treatment Committee (ATP-III) and the National Cholesterol Education Program (NCEP) recommend an LDL level of 100 mg/dl. The SPARCL study suggests that statin use significantly reduces the risk of stroke. There are several benefits of statin therapy in ischaemic stroke, but intracerebral haemorrhage associated with high doses (Amarenco *et al.*, 2009; Dimmitt et al., 2020; Szarek *et al.*, 2020). There are differential effects of lipids

on haemorrhagic and ischaemic stroke, with high cholesterol associated with ischemic stroke and low Cholesterol associated with haemorrhagic stroke (Dimmitt *et al.*, 2020; Leoncini *et al.*, 2013; Szarek *et al.*, 2020).

In a meta-analysis, sodium intake was reduced to 1800 mg per day, SBP was 2 mmHg, and DBP was 2 mmHg. shown to have decreased. It reduces BP by 1 mmHg in non-hypertensive patients and by 5 mmHg (SBP) and 2.7 mmHg (DBP) in hypertensive patients. Mediterranean diet protects against stroke and other cardiovascular disease (Olowoyo *et al.*, 2021; Paterson *et al.*, 2018).
Heavy alcohol consumption is a known risk factor for stroke (Li *et al.,* 2021*;* Zhang *et al.,* 2014). There is a J-shaped dose-dependent association between alcohol consumption and ischaemic stroke. A detailed analysis of twenty-five research finding on infarctive stroke and eleven on ICH and SAH found that low dose alcohol intake were protective against ischaemic stroke, whereas high alcohol intake was shown to be associated with a higher risk of ischaemic stroke. In addition, among the haemorrhagic stroke subtypes, low and high alcohol intake were related to increased occurrence of bleeding (Larsson *et al.*, 2016). Reynolds et al. reveals that taking 60 grams of alcohol per day was shown to increase the relative risk of all stroke, while consuming less than 12 grams of alcohol per day, or between 12 and 24 grams of alcohol, was shown to decrease the relative risk of ischaemic stroke *(K et al., 2003).* A previous study revealed that taking more than 300g of alcohol weekly, increased the likelihood of bleeding in the brain (*Casolla et al., 2012*).
Preventive strategies towards reducing aforementioned risk factors are key in preventing and reducing stroke occurrence in our society (Okon *et al.,* 2015; Olowoyo *et al.*, 2021).

2.3: Role of neuro-imaging in stroke diagnosis

Neuro-imaging is key to diagnosis and optimization of stroke care (El-Koussy *et al.,* 2014; Menon *et al.*, 2015). Multimodal Computed Tomography (CT) comprise of non-contrast CT, CT Angiography (CTA), CT perfusion (CTP). Brain Magnetic Resonance Imaging (MRI) modalities available are T1 weighted, T2 weighted, Fluid-Attenuated Inversion Recovery (FLAIR), gradient–recalled

susceptibility-weighed (GRSW) imaging, Diffusion-weighted imaging (DWI), apparent diffusion coefficient (ADC) maps, MR perfusion imaging, MR angiography (MRA) and contrast enhanced (CEMRA) (Menon *et al.*, 2015).

2.4: Cranial computed tomography (CT) in acute stroke

The primary role of cranial CT in acute stroke management is to exclude haemorrhage and stroke mimics. The presence and level of haemoglobin as measured by Hounsfield Unit (HU) is key in the visualization of haemorrhagic stroke. HU value at various tissues in the body are Air (-1000), Fat (-100), Cerebrospinal fluid(15), White Matter (43), Grey Matter(45), Intra cerebral haemorrhage (100), Calcium(1000) (Menon, 2020). Generally, HU value between 60-100 is seen in haemorrhagic stroke as whiter tissue named hyper-dense than normal brain with 40-45 HU (Liberman and Prabhakaran, 2017; Menon *et al.*, 2015). In brain tissue, acute haemorrhages are dense, subacute haemorrhages are dense, and chronic haemorrhages are sparse (Vilela and Rowley, 2017). Intravenous contrast is very useful in highlighting blood vessel or vascular lesion but its use is associated with adverse effect like renal impairments (Liberman and Prabhakaran, 2017; Menon, 2020; Villanueva-Meyer *et al.*, 2017). The immediate ischaemic changes on CT include loss of cortical and sub-cortical grey and white matter differentiation, loss of lentiform nucleus, effacement of sulci, squashing the ventricle, loss of insular ribbon, hyper-dense middle cerebral Artery sign and dot sign (Liberman and Prabhakaran, 2017; Thomassen *et al.*, 2008). The Alberta Stroke Program Early Computed Tomography Score (ASPECTS) has been used extensively to describe the extent and region of the brain affected by stroke (Kuang *et al.*, 2020; Wolff *et al.*, 2021). Hyperdense artery sign can be classified as proximal hyper-dense MCA sign and distal hyper-dense MCA sign (DOT sign) based on location of occlusion (Barber *et al.,* 2001*;* Noh*,* 2021). Cranial tomography angiography and CTP are useful in providing information regarding vessel patency and the haemodynamic reperfusion of a possible vessel occlusion (Menon *et al.*, 2015; Wannamaker *et al.,* 2019).

Cranial tomography angiography detects proximal occlusion of arterial

circulation as a sudden loss of contrast capacity and allows for effective visualization of proximal and distal end of occlusion. Cranial tomography angiography are helpful in ensuring adequate detection of proximal occlusion (Farzin *et al.*, 2016; Wannamaker *et al.,* 2019). Cranial tomography perfusion utilize bolus-tracking methods like conventional Perfusion-Weighted MRI (PWI) technique with three parameters routinely assessed namely Cerebral Blood Flow (CBF), Cerebral Blood Volume (CBV), and Mean Transit Time. CBF is minimally reduced, whereas peripheral ischemia maintains and increases CBV due to blood movement and relative collapse of the intravascular space to the nucleus. Mean transit times reflect long-term flow in both large vessels and the microcirculation (Wannamaker *et al.*, 2019).

Insufficient arterial blood flow results in abnormal venous patency and collapse, which can also lead to increased downstream resistance and decreased cerebral perfusion pressure, manifesting in CTP as CBV collapse. Discordant areas in neuroimaging, particularly CT and MRI, represent a mismatch between areas at risk of reparable compromise and areas already progressing toward irreversible compromise (Taylor *et al.,* 2014; Wannamaker *et al.*, 2019). Cranial tomography angiography is a relatively non-invasive technique that combines helical CT scanning with contrast enhancement to obtain vascular images. The merits of CTA in haemorrhagic stroke lies in its ability to detect perturbations and complex flow patterns and detection of narrowing in patient in subarachnoid haemorrhage. Cranial tomography angiography is limited in function by the need for contrast and ionizing radiation utilization especially in patient with renal impairment and contrast allergy (Menon, 2020).

2.5: MRI in acute stroke

The available MRI techniques in stroke include T1 and T2 weighed, ultra-fast MRI sequence FLAIR, GRSW, DWI, ADC, MR perfusion imaging, MRA and CEMRA (Althaus *et al.*, 2021; Vilela and Rowley, 2017). The physiology behind MRI acquisition follow the sequence of ischemia, sodium potassium channel failure, cytotoxic oedema, narrowing of extra-cellular matrix, restricted

diffusion of water within the cell and increased signal which can be measured by DWI (Althaus *et al.*, 2021; Vilela and Rowley, 2017). The DWI potentially discriminate between salvageable and irreversibly damaged tissues before therapy (Vilela and Rowley, 2017). It can detect cerebral ischemia within minutes of stroke onset compared to cranial CT that only detect ischemia after hours of stroke onset. Diffusion-weighted imaging is more sensitive due to its ability to display areas of hyperacute ischemia brightly, areas of old ischemia low intensity, and rapidly display ischemic areas throughout the brain (Jiang *et al.*, 2020; Yoshimoto *et al.,* 2019). Diffusion weighted imaging is based on ADC measurements, initially thought to be the ischemic core of irreversible damage, but its abnormalities may recover in few cases. However, due to cytotoxic oedema, in later stages ADC may return to baseline and rise showing occurrence of oedema that are vasogenic in nature (Vilela and Rowley, 2017).

Adding information from PWI to that obtained from DWI has been the cornerstone of principle of mismatch for selecting reperfusion candidates for acute stroke (Althaus *et al.*, 2021; Chen and Steckner, 2017; Vilela and Rowley, 2017). Diffusion-weighted imaging shows the area, whereas PWI reflects the entire area of hypoperfusion as it is irreversibly damaged by infarction. increase. The difference between the two volumes does not match, implying the presence of a penumbra. If there is no difference between PWI and DWI, there is no penumbra. Patients with acute stroke lasting more than 3 hours usually do not receive intravenous thrombolysis. However, recent studies have shown that intravenous thrombolysis may benefit carefully selected patients after PWI/DWI discord beyond the 3-hour window. In summary, multimodal MRA, DWI, PWI MRI, and FLAIR are required to detect discrepancies that identify areas of potentially reversible damage. Diffusion-weighted imaging is useful in confirming diagnosis of acute infarct and can reveal alterations in other neurological processes, from tumors to neurodegenerative diseases (Menon, 2020; Vilela and Rowley, 2017). The ability of DWI function to detect brainstem function in the first hours after stroke onset is limited. Activity of DWI are limited in watershed infarct (Yoshimoto *et al.,* 2019). PWI can be used to measure cerebral capillary perfusion. Passage of a contrast bolus results in a

non-linear decrease in signal with respect to cerebral perfused blood volume, thus identifying areas of hypoperfusion and reversible ischemia in contrast to DWI (Jiang *et al.,* 2020). Perfusion-weighted MRI varies, but the peak arrival time map automatically generated by the scanner is most commonly used. Peak arrival time is similar to mean transit time but remains an inadequate detector of tissue at risk.

Changes notice on MRI of haemorrhagic stroke patients are time dependent and it remains one of the surprising aspects of neuroimaging because the changes are primarily due to the changes haemoglobin undergo in tissues and the strength of magnetic fields. Head CT is sensitive for detecting acute intracranial haemorrhage, but additional MRI sequences improved the acute haemorrhage tendency (Farzin *et al.,* 2016). First, oxyhaemoglobin is converted to deoxyhaemoglobin within the first few hours. Then deoxyhemoglobin he converts to methaemoglobin within 72 hours. And intracellular haemoglobin is transformed into extracellular haemoglobin within a week, within a month, and finally into haemosiderin after a month. The appearance of the haemorrhage varies from MRI sequence to MRI sequence because the type of haemoglobin produced at each stage is different (Vilela and Rowley, 2017). MRI is isointense in T1-weighted and hyperintense in T2-weighted with oxyhaemoglobin, whereas his MRI at 3 days is hypointense in both T1 and T2 with deoxyhaemoglobin. Within 3 to 7 days, intracellular methaemoglobin causes MRI to be hyperintense on T1-weighted images and hypointense on T2-weighted images. Also, MRI is hyperintense in both T1 and T2 weights due to extracellular methaemoglobin. Finally, in the chronic phase, hemosiderin leads to T1-weighted hypointense and T2-weighted hyperintense (Althaus *et al.,* 2021). Ultrasound and digital subtraction angiography improve diagnostic characteristics of CT especially in people with CT negative subarachnoid and young adults.

2.6: Pathophysiology of Stroke

Cardiac embolism, arterial embolism, thrombosis, and hypoperfusion have been identified as mechanisms of ischaemic in acute stroke *(*Chen *et al.,* 2016;

Mbabuike *et al.,* 2017*).* The blockade resulting from these above mechanisms is the formation of the umbra and penumbra (Wannamaker *et al.,* 2019*).* After vascular occlusion, the major factors that ultimately determine tissue outcome are sectional CBF and length of vascular occlusion *(*Chen *et al.,* 2016; Kuriakose and Xiao, 2020*).* Normal CBF is 50-55 ml/min per 100 g brain. Ideally, neuronal integrity and function are maintained at a blood flow of 23 ml/100 mg/min and are well compensated by autoregulatory processes even when blood flow falls below 20-25 ml per 100 g/min (Zöllner *et al*., 2021). Oxygen extraction begins below CBF 18-20 mL/100 g/min, cell membrane disruption begins below CBF 12 mL/100 g/min, and finally irreversible neuronal cell death occurs at 6-8 mL/100g /min (Kuriakose and Xiao, 2020; Rabinstein, 2020). The ischaemic core corresponds to CBF values from 7 ml/100 g/min to 12 ml/100 g/min. The ischaemic penumbra correlates to an upper CBF limit of 17-22 mL/100 g/min and a lower CBF limit of 7-12 mL/100 g/min *(*Kuriakose and Xiao, 2020*).* The umbra is the ischaemic nucleus and represents the portion of brain tissue that cannot be salvaged, whereas the penumbra represents tissue that is functional, impaired and therefore salvageable. The goal of reperfusion therapy in acute stroke is to rescue this tissue by returning tissue flow to non-ischemic levels (Y *et al*., 2021).

At the cellular level, the biochemical and electrophysiological mechanisms involved in ischemic brain injury differ according to the degree of cerebral ischemia. Neuronal cell loss occurs because of two main mechanisms namely necrosis and apoptosis *(Y et al., 2021).* Necrosis occurs majorly in the hyperacute phase with ischemia in central region which occurs mainly as a result of disturbances in the normal homeostasis within cell. This is now followed by cellular swelling, membrane lysis, inflammation, vascular damage, and oedema formation. While necrosis is mainly seen in the umbra, apoptosis is responsible for neuronal death in the penumbra (Kuriakose and Xiao, 2020; Mbabuika *et al.,* 2017; Paciaroni *et al.,* 2009*).* The ischaemic cascade that occurs after blood flow compromise are dysfunction of the sodium-potassium pump, neuronal membrane depolarization, excitatory neurotransmitters release, activation of nNOS, calcium dependent enzymes, metabolite of

arachidonic pathway, superoxide dismutase and opening of calcium ion channels *(*Chen *et al.,* 2016; Kuriakose and Xiao, 2020; Yang *et al.,* 2018*).* Another important mechanism of brain infarction is Cortical Spreading Depolarization (CSD) which is linked to excessive glutamate release and imbalance in ionic activity leading to excessive depolarization of neurons. Cortical spreading depolarization enlarges the area of the severe umbra, thus allowing stronger infarct growth. Pathophysiology of stroke includes energy deficiency, loss of cellular ionic homeostasis, acidosis, elevated intracellular calcium levels, excitotoxicity, free radical-mediated toxicity, formation of arachidonic acid products, cytokine-mediated cytotoxicity, complement activation and multiple processes are involved, including glial cell activation and leukocyte infiltration (Gauberti *et al.*, 2016; S. Huang *et al.*, 2022; Kuriakose and Xiao, 2020).

Plaque build-up can eventually lead to narrowing of the vessel lumen and thrombus formation, leading to thrombotic stroke. In embolic stroke, an embolism occurs due to reduced blood flow to a blood area. Furthermore, activation of microglia and astrocytes, release of cytokines, chemokines and matrix metalloproteases, infiltration of neutrophils and other inflammatory cells are part of the inflammatory response leading to neuronal cell death and expansion of the infarct area. Overall, thromboembolic events, the concept of umbra and penumbra, oxygen and glucose starvation, CSD, inflammatory cascades, and neutron transmitter release are all hallmarks of ischemic stroke development *(*Fu *et al.*, 2021).

Regardless of the cause of haemorrhagic stroke, the haematoma that forms destroys glial cells, causing ischemia, neurotransmitter release, mitochondrial dysfunction, and cellular swelling. Thrombin activates microglia, causing inflammation and oedema *(*An *et al.,* 2017*).* The main damage is due to hematoma compression and increased intracranial pressure *(*Aronowski and Zhao, 2011). Secondary damage is caused by inflammation, blood-brain barrier disruption, oedema, overproduction of free radicals such as reactive oxygen species (ROS), glutamate-induced excitotoxicity, and release of haemoglobin

and iron from thrombi (Aronowski and Zhao, 2011; Righy *et al.*, 2016).

2.7: Stroke Induced Seizures and Epilepsy

Stroke is the leading cause of seizures in the elderly and has social and psychological consequences (Graham *et al.*, 2013b). Structural abnormalities, brain volume reduction, and scarring of the hypoxic-ischaemic brain are associated with epilepsy. Prospective studies show that 2-6% of stroke patients develop epilepsy during their lifetime (Hassani *et al.*, 2019; Lahti *et al.*, 2017). These proportions also vary between populations and by follow-up period. A meta-analysis of 34 longitudinal cohort studies involving 102,008 patients found a pooled incidence of SIS of 7%, compared with an SIE rate of 5% (Zou *et al.*, 2015b). A recent study of 1101 stroke survivors in Ghana found a prevalence of SIE of 11.4%, with male sex, cortical infarction, and elevated blood pressure considered predictors, and the use of antihypertensive drugs. use was found to prevent SIE (Sarfo *et al.*, 2020).

Identified mechanisms of SIS include alterations in neurotransmission, changes in intracellular ions, downregulation of GABAergic intracortical inhibition, activation of NMDA receptors, and elevated glutamate levels (Xu, 2018). These are all due to global hypoperfusion and cortical hyperexcitation due to ischemic effects. An initial decrease in blood flow results in a subsequent cytotoxic effect with intracellular calcium and sodium accumulation, resulting in depolarization of the cell membrane and lowering of seizure threshold. In addition, metabolic alterations such as accumulation of hemosiderin, loss of the GABA inhibitor pathway, acute glutamate release, and anaerobic depolarization also occur (Sarecka-Hujar and Kopyta, 2018). When a stroke occurs, nerve cell damage can have many causes, including Hypoxia, metabolic disorders, and acute Blood-Brain Barrier (BBB) disruption. These can cause early seizures (Yang *et al.,* 2018).

However, the mechanisms behind late seizures are different and can be secondary to scarring, chronic inflammation, angiogenesis, neurodegeneration, neurogenesis, axonal and synaptic sprouting, selective neuronal loss, and

altered synaptic plasticity (Sarecka-Hujar and Kopyta, 2018; Xu, 2018). The role of other epileptogenic mechanisms, such as kindling, needs confirmation. It is being proposed that after disruption of BBB that leukocytes invade into sites of cerebral legion, to induce cerebral neurons. Leukocytosis a marker of cerebral inflammation is associated with ictogenesis and epileptogenesis by changing sensitivity of ionic channel, modulation of glia cell and alteration of neurotransmitter.

There are widely reported controversies with regards to use of AEDs for primary prevention, underestimation, and the fact that there is no consensus regarding the most effective AEDs, for the treatment of SIE despite its rising burden and diagnostic challenges. Overall stroke volume, stroke size, cortical involvement, worse stroke severity score at presentation and evidence of ongoing infection, time of seizure onset are the identified predictor of SIS from available studies on SIS/SIE

2.8: Pathophysiology of Epilepsy

It is best described by imbalance in the activity of neurotransmitter through enhancement of excitation and/or inhibition of neurotransmission and receptors with attending effect on voltage gated ion channel.

2.9: Epileptogenesis

Epileptogenesis is defined as a molecular and cellular process of converting a less susceptible brain to one that is highly excitable leading to recurrent seizures (Pitkänen *et al.*, 2015). The exact pathogenic mechanism of SIE has not been elucidated; however, recent evidence suggests immunological and inflammatory processes. Observable alterations include molecular reorganization of membrane and extramembrane proteins, neuronal loss, gliosis, axonal dendritic and mossy fibre sprouting. The hippocampal circuitry consists of a trisynaptic excitatory pathway which starts from the entorhinal cortex to the dentate granule cells, which project to the CA1 region through Schaffer collaterals. There are local circuits in each region with excitatory and inhibitory interneurons (Rana and Musto, 2018).

There is well coordinated communication between the hippocampus and entorhinal cortex formed by multiple re-entrant best exemplified by the dentate gate theory between the entorhinal cortex and area CA3 and the temporoammonic pathway between the entorhinal cortex and area CA1. The gate regulates influx of dentate excitatory input from the entorhinal cortex into the hippocampus (Goldberg & Coulter, 2013; Hsu, 2007; Wong, 2013*)*. Dentate gyrus projects to hippocampal sub-region CornusAmmonis (CA) 3, CA3 projects to hippocampal sub-region CornuAmmonis 1 (CA1) and CA1 outputs back to the entorhinal cortex. Disruption of the function of dentate gyrus has been hypothesized to promote development of epileptogenesis in temporal lobe epilepsy (Goldberg and Coulter, 2013; Wong, 2013). Disrupting the regulatory function of dentate gate is associated with alteration of the mammalian target of rapamycin complex 1 (mTORC1) pathway within dentate gyrus granule cells that (Pun *et al*., 2012; Wong, 2013). The mTORC1 has linked to a lot regulatory pathways that enhance epileptogenesis (Wong, 2013).

2.10: Role of Voltage Gated Channels In Epileptogenesis

Voltage gated ion channels are central to the pathophysiology of epileptic seizures, for example, AEDs, like phenytoin, CBZ, and lamotrigine which are inhibitors of voltage gated sodium channel function (Lasoń *et al.,* 2013; Xiao et al., 2018). Genetic mutations related to the development of epilepsy were discovered mostly in the SCN1A and SCN2A gene encoding the Nav1.1 and Nav 1.2 core protein respectively (Camfield and Camfield, 2015; Xiao *et al*., 2018). Several mutated voltage gated sodium genes lead to inherited epileptic syndrome, Dravet syndrome (Severe myoclonic epilepsy of infancy), benign neonatal-infantile familial seizures, simple febrile seizures, and generalized epilepsy with febrile seizures plus (GEFS+) (Abdelsayed and Sokolov, 2013; Catarino *et al*., 2011).

Potassium channels are important for the process of repolarization and hyperpolarization that are key in development of seizures. Specifically, benign neonatal epilepsy. Furthermore, retigabine, a new AED focus potassium

channel to achieve is aim (Armijo *et al.,* 2000*).* Two potassium-channel subunits (KCNQ2 and KCNQ3) contribute to the M current (so-called because it is inhibited by the activation of muscarinic acetylcholine) and mutations of either of the genes encoding these subunits located at the 20q13 and 8q24 chromosomal loci, respectively lead to benign neonatal familial convulsions (Gunthorpe *et al.,* 2012*).*

Finally, concerning calcium channels, there are increasing data implicating both high- and low-voltage-activated calcium channels and their ancillary subunits in epilepsy (Zamponi *et al.*, 2010). The most important calcium channels are the P/Q high voltage type and the T type low voltage type *(*Zamponi *et al.,* 2010*).* T-type calcium channels play an important role in the network circuits formed by thalamic relay neurons, reticular nuclei of the thalamus, and neocortical pyramidal cells that sustain the firing of oscillatory bursts. Underlying Mechanism of Absence Seizures (Kim *et al.,* 2014; Seo & Leitch, 2014*).* Disruption of T type calcium channels is responsible absence seizures (Armijo *et al.,* 2000; Zampon*i et al.,* 2010*).* The anti-absence effect of ethosuximide is due to inhibition of her T-type Ca2+ channels in the thalamus *(*Armijo *et al.,* 2000; Zamponi *et al.,* 2010*).* P/Q type of calcium channels is key in ensuring fast transmission at synapsis. Mutation of P/Q channels is associated with epilepsy and other neurological issues like cerebellar ataxia, migraine with hemiplegia and vertigo *(*Zamponi *et al.,* 2010*).*

2.11: Role of Gamma Aminobutyric Acid (GABA) in Epileptogenesis

GABA is the chief inhibitory neurotransmitter in the mammalian central nervous system (Greenfield, 2013*).* It exerts its effect through ionotropic GABAA receptors and metabotropic G-protein-coupled GABAB receptors (Hirose, 2014). Activation of GABAA receptors produces chloride dependent fast inhibitory synaptic inhibition, while GABAB receptors induces potassium dependent hyperpolarization, slow inhibitory post synaptic potentials, inhibition of voltage-gated calcium currents thus interfere with release of neurotransmitters (Meldrum and Rogawski, 2007).

Disruption of GABA inhibitory activities is a an essential cause of epilepsy and seizures (Greenfield, 2013*).* Malfunction of GABAA inhibition has long been recognized in seizure genesis but the role of GABAB receptors in controlling seizure activity is still not well understood (Greenfield, 2013; Macdonald *et al.,* 2010*).* Mutations in both translated and untranslated inhibitory GABAA receptor subunit genes are responsible for genetic basis for epilepsy syndrome like childhood absence epilepsy, juvenile myoclonic epilepsy, pure febrile seizures, generalized epilepsy with febrile seizures plus, and Dravet syndrome *(*Hirose, 2014; Macdonald *et al.*, 2010*).*

2.12: Role of Glutamate in Epileptogenesis

The glutamate released from synapsis is a key excitatory neurotransmitter that useful in generating and spreading epileptic discharges (Alexander and Godwin, 2006*).* It act on N-Methyl-D-aspartate (NMDA), ionotropic and metabotropic receptors appears to play a major role in the initiation and spread of seizure activity and modulates epigenetic and genetic activities of neurotransmitters (Niswender and Conn, 2010).

Paroxysmal depolarization shifts are intracellular recordings in epileptic foci during spiking discharges (Armijo *et al.*, 2000; Greenfield, 2013).

2.13: Classification of Antiepileptic Drugs based on mechanism of action

Therapeutic strategies for epilepsy include modification of inhibitory and excitatory mechanism of neurotransmission. However, many AEDs work through multiple mechanisms. Antiepileptic drugs that work by blocking Na+-dependent action potentials include Phenytoin, CBZ, Lamotrigine, Topiramate, and Zonisamide.

Sodium ions exist in three states: dormant, active, and inactive. Sodium (Na) activities are dependent on the state of a channel, while Na channel in the active state allow influx of ion, the channel remain close in inactive state. It is however, important to state that at resting, there is movement of Na across the cell but this becomes aggravated during active state (Wei *et al.*, 2017*).* While these channels represent action potentials, they are in an active state, allowing

Na ion influx. After activation or stimulation, some of these sodium channels become inactive for a period called the refractory period. Antiepileptic drugs that target Na channels prevent the channel from reverting to its active state by stabilizing its inactive form, thereby preventing axons from repeatedly firing.

Presynaptic and postsynaptic blockade of axonal Na channels stabilizes neural membranes, blocks and prevents post-tetanic potentiation, limits the onset of peak seizure activity, and reduces seizure propagation *(*Abou-Khalil, 2016a).
Voltage-gated calcium channel blockers include phenytoin and sodium valproate. Ethosuximide and valproic acid act by blocking her T-type calcium channels in thalamic neurons. On the other hand, lamotrigine decreases glutamate release, whereas benzodiazepines and barbiturates increase GABA receptor action. Sodium valproate, gabapentin, and tiagabine work by increasing the availability of GABA. Synaptic vesicle protein 2A (SV2A) is widely present in the brain and helps to coordinate neurotransmitter release from vesicle. Inhibition of SV2A leads to a significant reduction in action potential, neurotransmission and secondarily affect the level of Calcium. Levetiracetam interferes with SV2A to ensure its antiepileptic and other neuroprotective properties *(*Svalheim *et al.,* 2008: Svalheim *et al*., 2009*).*

2.14: Carbamazepine (CBZ)

Carbamazepine (CBZ) is an important AED for focal and generalized epilepsy *(*Huang *et al.,* 2015*).* It is useful as trigeminal neuralgia and bipolar disorder. Carbamazepine work by interfering with activity of sodium channel during process of generation of membrane potential, thus, preventing repetitive or excessive firing *(*Nevitt *et al.,* 2019*).* It is not soluble in water, thus best given orally. Autoinduction, pronounced plasma protein binding and liver metabolism are the major pharmacokinetic highlights of CBZ. It is metabolized into CBZ 10,11-epoxide by epoxidation and CBZ 10,11-trans-dihydrodiol by hydrolysis. Through auto-induction, it speeds up the metabolism of other drugs.

Adverse drug reactions associated with CBZ include agranulocytosis, Steven-Johnson syndrome, hepatotoxicity, thrombocytopenia, and drug interactions

due to inhibition of liver microenzymes. Rifampicin and other inducers such as grapefruit juice and St. John's wort may reduce CBZ levels. A new analogue of CBZ, oxcarbazepine (OXC), was specifically designed to limit the self-induction and drug-drug interaction effects of CBZ. Unlike CBZ, OXC does not generate epoxide metabolites, but exhibits similar activity to CBZ. OXC is almost completely absorbed when administered orally and can be taken with food. It has lesser Drug-Drug Interaction (DDI), better tolerability and fewer side effects compared to CBZ and it readily crosses the BBB.

2.15: Levetiracetam (LEV)

Levetiracetam (LEV) is a piracetam derivative (S-enantiomeric pyrrolidone), a relatively new broad-spectrum AED. It has an excellent pharmacokinetics viz, oral bioavailability, very low protein binding, no hepatic metabolism, half- life of 6-8 hours, 66% excreted unchanged in the urine and the rest is hydrolyzed to inactive compounds.

Its main mechanism of action is binding to the synaptic vesicle protein, SV2A, which results in nonspecific decrease in neurotransmitter release in a state of neuronal hyperactivation (Lyseng-Williamson, 2011). Levetiracetam modulate calcium ion release from Inositol-Triphosphate (IP3)-sensitive without interfering calcium storage. The favorable pharmacokinetics profile, and lower incidence of drug interactions when compared to other AEDs contribute to its growing use (Chakravarthi *et al.,* 2015; Shetty, 2013b). It is best started with 500 mg/d in two divided doses or once at bedtime with the extended release preparation, then can be titrated to 3000mg/d to 4000mg/d. In addition to this excellent pharmacokinetics and cognitive profile, there are no convincing data to support possible endocrine side effect of levetiracetam during treatment as previously reported in a study on animal subject (Abou-Khalil, 2016).

2.16: Non-pharmacological Therapy

Non-pharmacologic therapies include vagus nerve stimulation, acupuncture, ketogenic diets, and surgical intervention. The ketogenic diet is safe, has been very useful in management of refractory epilepsy especially in children

(*Freeman et.al 2007).*

The most successful treatment of epilepsy is with modern AEDs, which can achieve control of seizures in 70-80% cases.

2.17: Stroke outcome and severity

The National Institutes of Health Stroke Scale Score (NIHSS) has been used successfully as an instrument to assess stroke severity and predict outcome. It is a reliable instrument that has been validated and revalidated.

The Modified Rankin Scale (MRS) is an excellent instrument that has been used successfully to measure stroke outcome (Banks and Marotta, 2007*)*. Barthel Index (BI) can help plan rehabilitation strategies (Adams *et al.,* 1999; Leira *et al.*, 2008*)*.

CHAPTER THREE

METHODOLOGY

3.1: Study Sites

This study which comprises of three phases was carried out at University College Hospital (UCH), Ibadan, Oyo State, Federal Medical Centre, Abeokuta, (FMCA) and Olabisi Onabanjo University Teaching Hospital (OOUTH) Sagamu, Ogun State.

3.2: Study Design

The study comprised of retrospective phase, observational non-interventional phase, and prospective controlled clinical trials of LEV among Stroke Patients.

3.3: Duration

Prospective interventional phase comparing tolerability and efficacy of LEV and CBZ in the treatment or prevention required a two-year period of follow up of participants after enrolment. The retrospective phase evaluated pattern of epileptic patients over a period of 5 years beginning January 2014 until December 2018. Enrolment into the prospective phase began January 2019 after obtaining relevant approvals with the last patients completing the requisite two-year follow up in December 2021. Consequently, the study lasted three years from commencement until close out.

3.4: Study Population

Primary goal of these study was to explore pharmacotherapeutic intervention in reducing morbidity and mortality associated with stroke, therefore, individuals who suffered stroke and/or had been previously diagnosed with epilepsy were involved. Whereas study involving demographics of epilepsy was retrospective, stroke patients were enrolled, first as in-patient, and thereafter followed-up for a period of 24 months prospectively.

3.5: Sample size for hospital-based pattern of epilepsy among adult (and adolescent) Nigerians in South western Nigeria.

A total purposive sampling method was used in this phase of the study, as such all patient with epilepsy attending or that attended epilepsy clinic in three centres within last 5years were involved in the study.

3.6: Sample size for pattern and predictor of seizure disorders among stroke survivors

Sample size is determined Leslie Kish's Formula

$$N = \frac{P_1(1-P_1)\,(Z_\alpha)^2}{(D)^2} \qquad \text{Equation 3.1}$$

Where:

N= sample size that is desired

Z_α = standard normal distribution adjusted off with probability α normally placed at 1.96, which correlate to 95% CI

P_1= prevalence of SIE set at 25

$_D$= confidence interval

N = 288

The minimum sample size required was 288 patients, and a total of 346 patients were recruited after controlling for attrition rate of 20%.

3.7: Sample size for Comparative efficacy and tolerability of Levetiracetam and Carbamazepine in Seizure Induced Epilepsy

Ninety-two (92) patients who developed seizure out of the 346 patients from study two were recruited and randomly divided into two groups (LEV and CBZ).

3.8: Sample size for Evaluation of the role of Levetiracetam and Carbamazepine in the prevention of Stroke Induced Seizure/Stroke Induced Epilepsy.

Sample size was determined factoring in time to event formulae.

$$N = z_{1-\alpha/2} + z_\beta(1/1-p_1 + 1/1-p_2)$$

$(\log R)^2$ Equation 3.2

Where:

N= sample size that is desired

Z_α = standard normal distribution adjusted off with probability α normally placed at 1.96, which correlates to 95% CI

Z_β = the value of the standard normal distribution cutting off probability β, which is 1.28 for 90% power.

P_1= the fraction of participants on LEV without SIE

P_2 = the proportion of participants CBZ without SIE

$R = \ln p_1 / \ln p_2$

N = 192.

The minimum sample size required is 192, however factoring in 20% attrition (38 patients), 240 patients were recruited and subsequently divided into 80 each group of LEV, CBZ and None.

3.9: Source and Collection of Data for phase 1

Relevant case notes were obtained from respective health records department of the three hospitals with strict adherence to:

1. Participants aged 18 years and above who had attended/attending epilepsy clinics
2. Adequate documentation of clinical information including, at least one EEG report.

3.9.1: Conduct of phase 1

The hospital records of all participant visiting/had visited neurology between January 2014 with diagnosis of epilepsy were evaluated. Clinical and sociodemographic characteristics were extracted with special attention to medical history relating to the epilepsy including age, circumstances of onset, associated history of cardiovascular event like stroke, Traumatic Brain Injury (TBI) and perinatal/birth asphyxia and substance abuse. Demographics, sociobiological characteristics, clinical information, and neurophysiological findings of participants with SIE were extracted and compared with those with

Non-Stroke Induced Epilepsy (NSIE). Details of seizure onset, seizure type, seizure duration, other seizure characteristics, AEDs type and duration of use were also obtained in all cases, follow up clinical information including subsequent findings on further investigations, as well as outcomes were documented. Outcome measures used includes, demographic pattern, neurophysiological findings, and refractory epilepsy which were compared between participants.

3:10: Source and Collection of Data for first part of phase 2

3.10.1: Inclusion Criteria

1. All newly diagnosed stroke patients stroke using WHO criteria with neuroimaging confirmation of stroke
2. Informed Consent of participants and/or Caregiver obtained prior to enrolment and/or in the course of the study.

3.10.2: Exclusion Criteria

1. Evidence of stroke mimics, for example, subdural hematoma.
2. Known epileptic patient
3. Associated head injury

3.10.3: Withdrawal criteria

1 Withdrawal/refusal of consent

2 Failure to adhere management protocol

3.10.4: Conduct of Study

Patients who met inclusion criteria were enrolled at the three selected centres, UCH, Ibadan, FMC, Abeokuta and OOUTH, Sagamu. Demographics, history, and physical examination were done. Briefly, age, gender, clinical information including past medical history were obtained from each participant. Thereafter, physical examination with detailed neurological assessment including test of cognitive functions, as much as possible, were recorded in case record forms prepared for the purpose. Cranial CT scan or MRI was done in addition to other ancillary investigations. Relevant medical history, general physical and

neurological examination were conducted at regular interview during period of admission, and subsequently, monthly for three months and, at 6, 9, 12 and 24 months for survivors.

Post Stroke Outcome (PSO) such as severity, functional outcome, cognition and epileptiform pattern were assessed using National Institute of Health Stroke Scale (NIHSS), Modified Ranking Scale (MRS), Cognitive Screening Instrument for Dementia (CSID), and Electroencephalography (EEG), respectively. Development of PSE, Mortality Rate (MR) and determinants of PSE were evaluated. Medical care of each patient was in line with the standard of care for stroke patients including use of medications, for example, treatment of hypertension, appropriate nursing care and physiotherapy.

3.11: Source and collection of data for second part of phase 2

3.11.1: Inclusion Criteria

1. All participants in study 2 who developed seizure disorder during follow up
2. Patients with no history of allergic reaction to LEV or CBZ.

3.11.2: Exclusion Criteria

1. Refusal of consent
2. Patients with history of previous seizure before stroke

3.11.3: Withdrawal Criteria

1 Withdrawal of consent
2 Failure to adhere management protocol
3. Patients that developed allergic reaction to medication

3.11.4: Conduct of Study

Participants enrolled into this arm of the study met the definition of SIS or SIE and were openly randomized to receive LEV or CBZ at standard dose. Individuals with history of allergy to either study drugs were excluded. Full clerking especially neurological assessment was done at enrolment and subsequent visits. In addition, Treatment Emergent Symptoms and Signs

(TESS), was determined during each scheduled visit at 1, 3, 6, 12 15, 18, 21 and 24 months from date of enrolment into this arm of the study. For emphasis, LEV was administered at a dose of 250mg twice daily while CBZ was given at a dose 200mg twice daily. Stroke patients on follow up that developed SIS/SIE were openly randomized to receive either LEV group or CBZ after they were fully clerked. Participants were further assessed for drug-related adverse effects by TESS during each clinic visits. These patients were followed up for 24months by monitoring relevant parameters which include seizure control/ frequency, stroke severity assessed by NIHSS, functional outcome assessed the MRS, cognitive outcome measured by CSID, death, epileptiform pattern and other abnormalities on EEG and associated adverse effects of AED therapy. None of the participants developed significant adverse effect to warrant withdrawal. SIS was classified as symptomatic seizures occurring within 7days of ictus while SIE was defined as symptomatic seizures occurring after 7days ictus or recurrent seizures. For this study, seizures were diagnosed clinically.

3.12: Source and collection of data for phase 3

3.12.1: Inclusion Criteria

1. Newly diagnosed stroke patients without any prior history of seizures
2. Age 18 years and above
3. Informed consent

3.12.2: Exclusion Criteria

1. Stroke complicated by head injury.
2. Stroke patient with prior history of abuse of psychoactive substances
3. Background epilepsy disorder prior to stroke onset.

3.12.3: Withdrawal criteria

1. Withdrawal of consent
2. Failure to adhere to management protocol including non-adherence to medications. Adherence to protocol was assessed by feedback on

routine visits to hospital by the patients, and occasional home visits and phone call by trained research assistance.

3. Development of serious adverse drug reaction

3.12.4: Conduct of study

Newly diagnosed stroke patients with no history of seizure (and/or abnormal EEG findings) who satisfy inclusion criteria were enrolled into the study and followed up for a period of 12months. Eligible participants were allotted to receive either LEV or CBZ daily after documentation of relevant clinical information. In the study, history, physical and neurological examination was conducted for each participant. TESS, NIHSS, and MRS was administered at entry and at subsequent visits at 1, 3, 6, 12, 24 months.

3.13: Neuroimaging Protocol

Neuroimaging, (CT and or MRI) were acquired for participant that were recruited. An initial review was done immediately after acquiring pre-contrast images. While no contrast was given to haemorrhagic stroke cohort. the ischemic cohort were given 40mls of iodine-based Ultravist. The contrast was given intravenously very fast before post-contrast image were obtained. The ABC/2 method was used for estimating the volume for both haemorrhagic and ischaemic stroke (Sims *et al.*, 2009; Wannamaker *et al.*, 2019).

3.14: EEG Acquisition and Wave Changes Description Protocol

The EEG was performed using phoenix digital 16 channel machine and international standard 10-20 arrangement system in all participants. These procedures were done at presentation. 3months, 6months and 12months and taking about thirty minutes per session. Filter were adjusted at 70Hz but lowered to lower frequency to reduce interference.

3.15: Cognitive Screening Instrument for Dementia (CSID)

It is an acceptable global cognitive status assessment instrument which was created by Ibadan Indianapolis dementia research group (*Hall et al., 2000).* It assessing various domain of cognition ranging from memory, orientation,

language, and praxis. It has been used successfully in different disease condition including stroke (Akinyemi *et al.*, 2008).

3.16: Definition of terms

- Post Stroke Outcome (PSO) include severity, functional outcome, cognition and epileptiform pattern as measured by NIHSS, MRS, CSID, EEG, respectively.
- NIHSS was scored between the ranges (0) for no stroke and (42) for the most severe stroke.
- MRS 0, 1, 2 and 3 described as good outcome while MRS 4,5,6 described as having poor outcome.
- EEG waves acquisition, recording and reading was based on ILAE and standard neurophysiological criteria as follows:
    - Sharps were described as pointed peaks with length ranging between seventy (70)-two hundred (200) milliseconds which is clearly different from background EEG activities.
    - Slow waves were described as Theta rhythm measuring <4 – 7 Hz/s and Delta rhythm at frequencies <4Hz/s.
    - Epileptiform discharges were described as focal (spikes or sharps), sharps with associated slowing or spikes with associated slowing.
- Risk factors
    - Hypertension was defined as SBP ≥140mmhg and DBP ≥90mmhg and current use of BP-lowering agents.
    - Diabetes mellitus was defined as a Fasting Blood Glucose (FBG) ≥ 126mg/dl or glycated haemoglobin (HbA1c) > 6.5%, or current use of oral hypoglycaemic agents and or insulin.
    - Dyslipidaemia was defined as abnormalities in lipid as HDL ≤ 40mg/dl or LDL ≥ 100mg/dl or TC ≥ 150mg/dl following the NCEP guidelines. All the fasting blood samples were taken after an overnight fast of at least 8-12 hours.

3.17: Seizure description protocol and epileptiform pattern

SIS was defined as acute symptomatic seizures occurring after an acute stroke following ILAE recommendations. SIS was classified as seizures occurring within 7days of stroke onset while SIE was defined as recurrent seizures or occurrence of seizure after 7days of stroke ictus. Diagnosis of seizure was clinically.

3.18: Source and Brand of AEDs

The brand of LEV and CBZ used are from GLAXOSMITHLINE Nigeria. They are gotten from pharmacy department of each of the three participating centres. Patients that could not afford the medication were supported financially.

3.19: Data Analysis

The data were first entered and cleaned in Microsoft excel before transferring into Statistical Package for Social Science (SPSS) version 22 for analysis. The results were presented in figures and tables. Test for normality was checked for each variable to determine their normality. Number of participants that developed stroke or seizure was derived using descriptive and it was presented in number(percentage). Pearson chi-square was used to compare two categorical variables and presented in number(percentage). Comparing categorical and continuous variable, independent student t-test (or Mann-Whitney U) was used and Analysis of Variance (ANOVA) (or Kruskal-Wallis) where appropriate. Binary logistic regression was used to determine the predictors of seizure, epilepsy, ischaemic seizure, haemorrhagic seizure and mortality. Statistically significance was set at $p<0.05$.

CHAPTER FOUR

RESULTS

4.1: Socio-biological Characteristics of 946 Patients Treated at Selected Hospitals in South Western Nigeria for Epilepsy between January 2017 and December 2021

A total of 946 patients, comprising 448 females and 498 males, were seen and treated over a five-years period, between January 2017 and December 2021. Average duration of follow-up was 2years, and the mean age at diagnosis was (31.58±20.82). However, mean age for female at diagnosis was statistically significant (33.2±20.98 vs 35.14±21.10; p≤0.009).

A total of 205 (45.8%) and 53(11.8%) of male patients had tertiary and post graduate education respectively compared to 212(42.5%) and 41(8.2%) of female patients who had tertiary and post graduate education respectively and this was statistically significant (p≤0.004) (See Table 4.1).

Table 4.1: Socio-biological Characteristics of 946 Patients Treated at Selected Hospitals in South Western Nigeria for Epilepsy between January 2017 and December 2021

S/N	Variables	Male (n=448)	Female (n=498)	Total (n=946)	x^2 value	p-value
1	Age n (%)					
	18-35	221(49.3)	257(51.6)	478(50.5)	2.587	0.274
	36-60	166(37.1)	190(38.2)	356(37.6)		
	>60	61(13.6)	51(10.2)	112(11.8)		
2	Age of onset (mean±SD)	33.2±20.98	35.14±21.10	31.58±20.82	2.599	0.009*
3	Marital Status n (%)					
	Never married	190(42.4)	198(39.8)	388(41)	10.782	0.056
	Currently married	254(56.7)	286(57.4)	540(57.1)		
	Separated	1(0.2)	1(0.2)	2(0.2)		
	Widow/widower	0(0)	11(2.2)	11(1.2)		
	Cohabiting	1(0.2)	1(0.2)	2(0.2)		
	Divorce	2(0.4)	1(0.2)	3(0.3)		
4	Formal Education n (%)					
	None	17(3.8)	28(5.6)	45(4.8)	15.155	0.004*
	Primary	8(1.8)	29(5.8)	37(3.9)		
	Secondary	165(36.8)	188(37.8)	353(37.3)		
	Tertiary	205(45.8)	212(42.6)	417(44.1)		
	Post Graduate	53(11.8)	41(8.2)	94(9.9)		

*p<0.05 comparing male to female SD- Standard Deviation

4.2*:* Aetiology of Epilepsy among 946 Patients Treated at Selected Hospitals in South Western Nigeria for Epilepsy between January 2017 and December 2021

One hundred and sixty-four, that is 17.3%, of the 946 patients with epilepsy had background history of CVD. In the majority of cases, 569 (60.1%), there was no identifiable cause while metabolic, infectious, genetic, and immunologic disorders were the presumed causes in the remaining 141 (25%) patients (See Figure 4.1, 4.2).

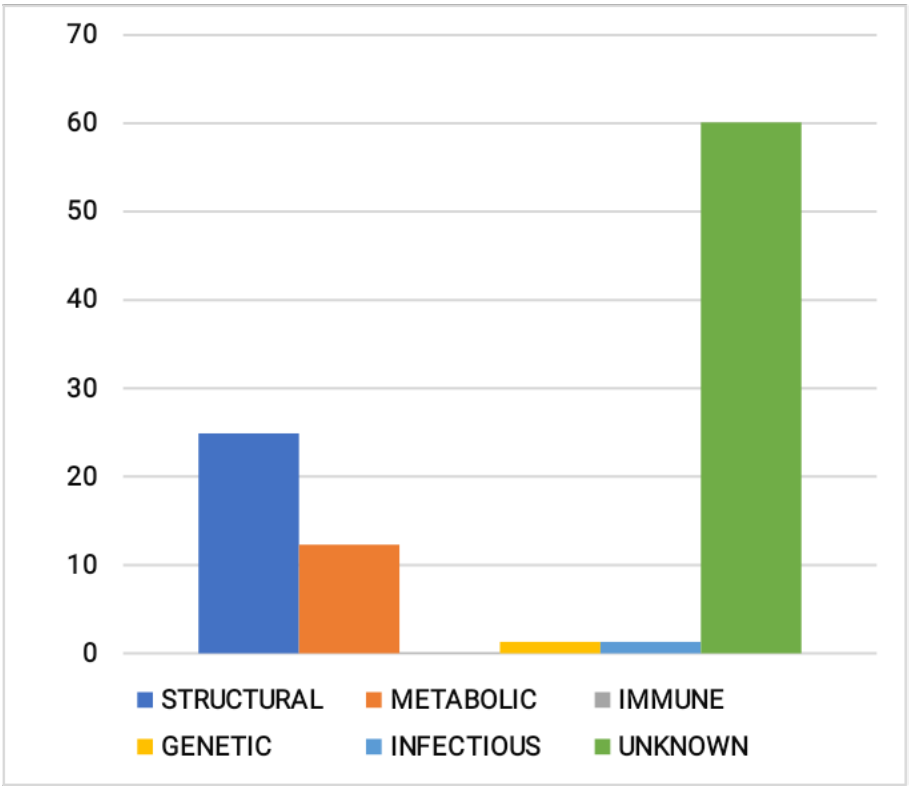

Figure 4.1: Aetiology of Epilepsy among 946 Patients Treated at Three Selected Hospitals in South Western Nigeria for Epilepsy between January 2017 to December 2021

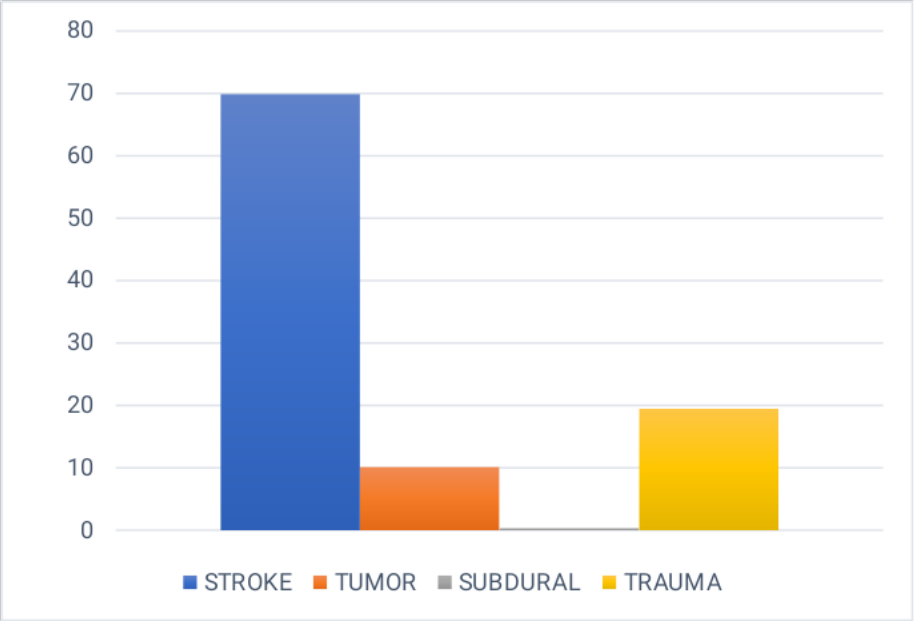

Figure 4.2: Subtype of Epilepsy among 236 Patients with Epilepsy of Structural Aetiology Treated at Selected Hospitals in South Western Nigeria for Epilepsy between January 2017 to December 2021

4.3: Comparison of Socio-biological Characteristics of 164 Stroke-induced

Epilepsy and 746 non-stroke Induced Epilepsy Treated at Selected Hospitals in South Western Nigeria between January 2017 to December 2021

The mean age of diagnosis among SIE was 53.12±16.80 years whereas mean age of participants with NSIE was 29.07±19.35 years; ($p<0.05$). The frequency of age among SIE group compared to NSIE group was [18-35 14(8.5%) vs 461(56.0%), 36-65 99(60%) vs 258(33.0%) and >65 52(31.5%) vs 62(7.9%), ($p\leq0.001$)]. Other details of sociobiological characteristics of stroke-induced epileptic patients in comparison with other epileptic patients are showed in Table 4.2.

Table 4.2: Socio-biological Characteristics of Stroke-Induced Epilepsy among the 946 Participants Treated at Selected Hospitals in South Western Nigeria between January 2017 and December 2021

Variables	Stroke n(%)	No Stroke n(%)	Total n(%)	X^2 Value	P Value
Gender					
Male	84(51.2)	363(46.4)	447(47.3)	1.234	0.267
Female	80(48.8)	419(53.6)	499(52.7)		
Age					
18-35	14(8.5)	461(59.0)	475(50.2)	160.329	<0.001*
36-65	99(60)	258(33.0)	357(37.7)		
>65	52(31.5)	62(7.9)	114(12.1)		
Formal Education					
None	13(7.9)	34(4.4)	47(5.0)	19.617	0.001*
Primary	15(9.1)	22(2.8)	37(3.9)		
Secondary	54(32.7)	298(38.2)	352(37.2)		
Tertiary	70(42.4)	346(44.3)	416(44)		
Postgraduate	13(7.9)	81(10.3)	94(9.9)		

*p<0.05 comparing stroke and no stroke

Table 4.3: Seizure Characteristics of Stroke-induced Epilepsy among the 946 Participants Treated at Selected Hospitals in South Western Nigeria between January 2017 and December 2021

Variables	Stroke n(%)	No Stroke n(%)	Total n (%)	X^2 Value	P Value
Seizure Onset (years)					
<1	46(27.9)	230(31.9)	336(35.5)	27.400	<0.001*
1-2	48(29.1)	113(15.7)	161(17.0)		
2-5	37(22.4)	139(19.3)	176(18.6)		
>5	34(20.6)	239(33.1)	273(28.9)		
Seizure Type					
Focal onset	40(24.2)	188(24.1)	228(24.1)	2.167	0.338
Generalized onset	123(74.5)	565(72.3)	688(72.7)		
Unknown onset	2(1.2)	28(3.6)	30(3.2)		
Type of Epilepsy					
Focal onset	25(15.2)	88(11.3)	113(12.0)	3.042	0.385
Generalized onset	114(69.1)	562(72.0)	676(71.5)		
Combined onset	22(13.3)	100(12.8)	122(12.9)		
Unclassified	4(2.4)	31(3.9)	35(3.6)		
Age of Onset	53.12±16.80	29.07±19.355		T test	<0.001*

	5			14.813	

*p<0.05 comparing stroke and no stroke

4.4: Comparison of the Background Wave Changes and Epileptiform Pattern on EEG among 164 Participants with Stroke Induced Epilepsy and 782 Epilepsy Patients without Stroke Treated at Three Selected Hospitals in South Western Nigeria

The background EEG changes of the 164 participants with SIE, revealed that 58(35.4%), 1(0.6%), 60(36.6%), 10(6.1%) 6(3.7%) 29(17.7%) had alpha, beta, theta, intermixed fast, intermixed slow and delta waves respectively on EEG compared to epilepsy patient without stroke with a value of 496(63.4),18(2.3),142(18.2), 82(10.5), 25(3.2) and 19(2.4) that had alpha, beta, theta, intermixed fast, intermixed slow and delta respectively and was statistically significant (p<0.001).

Furthermore, of the 164 participants with SIE, 100(61%), 31(18.9%), 5(3%), 28(17.1%) had generalized, focal, focal to secondary generalized and no epileptiform pattern compared to 782 epilepsy patients without stroke with value of 358(45.8%), 179(22.9%), 36(4.6%) and 209(26.7%) (p≤0.005).

The participant with SIE had 100(61%), 16(9.8%), 20(12.2%) 28(17.1%) respectively of generalized, focal, intermittent and no slowing on EEG compared to those without stroke with slowing of 354(45.3%), 53(6.8%), 327(41.8%), 48(6.1%) for generalized, focal, intermittent and No slowing on EEG (p<0.001) (See Table 4.5).

Table 4.4: Comparison of the Background Wave Changes and Epileptiform Pattern on EEG among 164 Participants with Stroke Induced Epilepsy and 782 Epilepsy Patients without Stroke Treated at Three Selected Hospitals in South Western Nigeria

Variables	Stroke n(%)	No Stroke n(%)	Total	X^2 Value	P Value
Background					
Alpha rhythm	58(35.4)	496(63.4)	554(58.6)	106.076	<0.001*
Beta rhythm	1(0.6)	18(2.3)	19(2.0)		
Theta rhythm	60(36.6)	142(18.2)	202(21.4)		
Intermixed fast	10(6.1)	82(10.5)	92(9.7)		
Intermixed slow	6(3.7)	25(3.2)	31(3.2)		
Delta rhythm	29(17.7)	19(2.4)	48(5.1)		
EEG Slowing					
Generalized	100(61)	354(45.3)	454(48.0)	38.104	<0.001*
Focal	16(9.8)	53(6.8)	69(7.3)		
None	28(17.1)	327(41.8)	355(37.5)		
Intermittent	20(12.2)	48(6.1)	68(7.2)		
Epileptiform					
Generalized	100(61)	358(45.8)	458(48.4)	12.971	0.005*
Focal	31(18.9)	179(22.9)	210(22.2)		
Focal to generalized	5(3)	36(4.6)	41(4.3)		
None	28(17.1)	209(26.7)	237(25.1)		

*p<0.05 comparing stroke and no stroke

4.5: Medication pattern among 946 Participants Treated at Selected Hospital in South Western Nigeria between January 2017 to December 2021

Of the 946 epilepsy patients recruited, 652(68.9%) patients were on medications [monotherapy 514(54.3%) and polytherapy 138(14.6%)] while 294(31.1%) patients were not on medications. Concerning type of AEDs prescribed, 85(13.0%), 515(79.0%), 21(3.2%), 22(3.4%) and 9(1.4%) respectively were on LEV, CBZ, phenytoin, valproate, and phenobarbital (PHB) respectively (See Figure 4.3, 4.4).

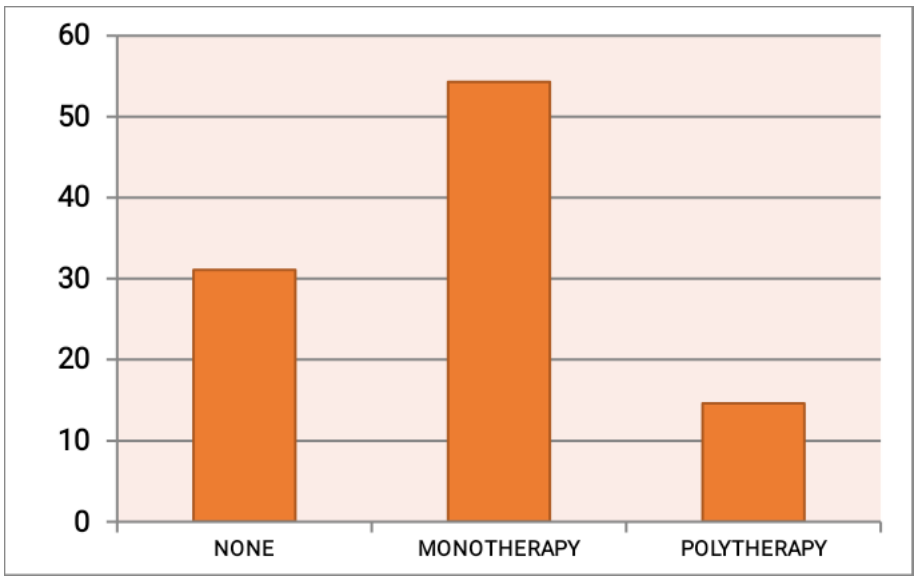

Figure 4.3: Pattern of number of medications use among 946 Patients Treated at three Selected Hospitals from January 2017 to December 2021.

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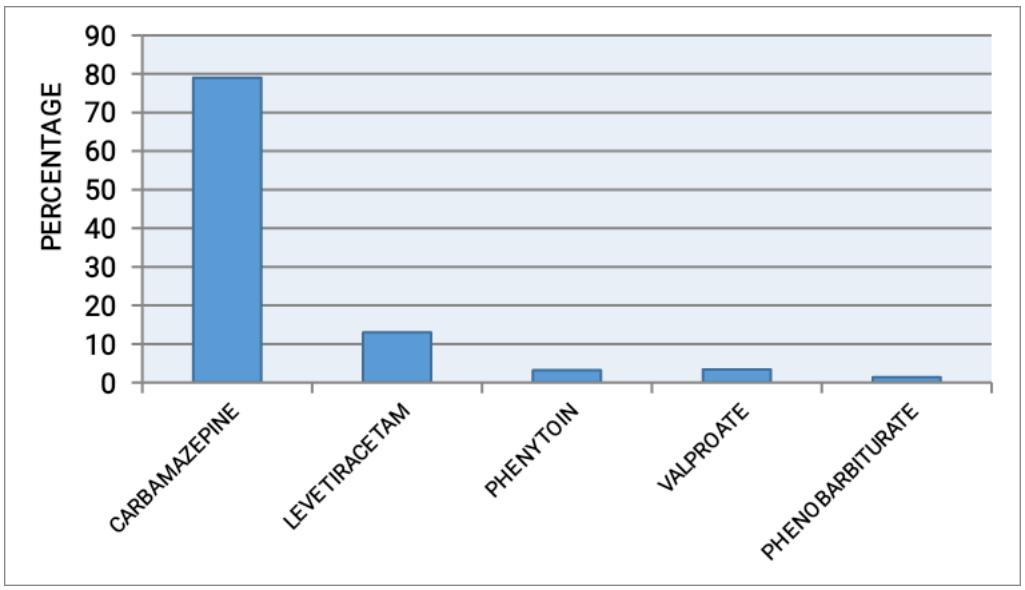

Figure 4.4: Distribution of AEDs prescribed among 652 Patients on medication Treated at Three Selected Hospitals from January 2017 to December 2021.

AEDs – Anti Epileptic Drugs

4.6: Socio-biological Characteristics of 346 Stroke Patients with Stroke Induced Seizure and Stroke Induced Epilepsy Treated at Three selected Hospitals in South Western Nigeria for a period of two years

Of the 346 stroke patients recruited into the study, 199(58.0%) were males while 147(42.0%) were females. A total of 258(74%) of the participants had ischemic stroke while 88(26%) had haemorrhagic stroke. Out of the 258 ischemic stroke participants, 146(56.6%) were males and 112(43.4%) were females. Furthermore, of the 88 participants with haemorrhagic stroke, 53(60.2%) are males and 35(39.8%) are females. Ninety-two (27%) of the 346 participants developed seizures. Twenty-six of 88(29.5) individuals who had haemorrhagic developed seizure disorder whereas seizure was recorded among 66 of the 258 individuals who had ischemic stroke, (29.5% vs 25.6%). There were 24(26%) and 68 (74%) with SIS and SIE respectively (See Figure 4.5 to 4.8).

Furthermore, 254(73%) of the participant had no seizure, of the 92 patients that develop seizure 24(26%), 32(35%), 36(36%) had seizures only, seizure to epilepsy and epilepsy only respectively (See Figure 4.9 to 4.10).

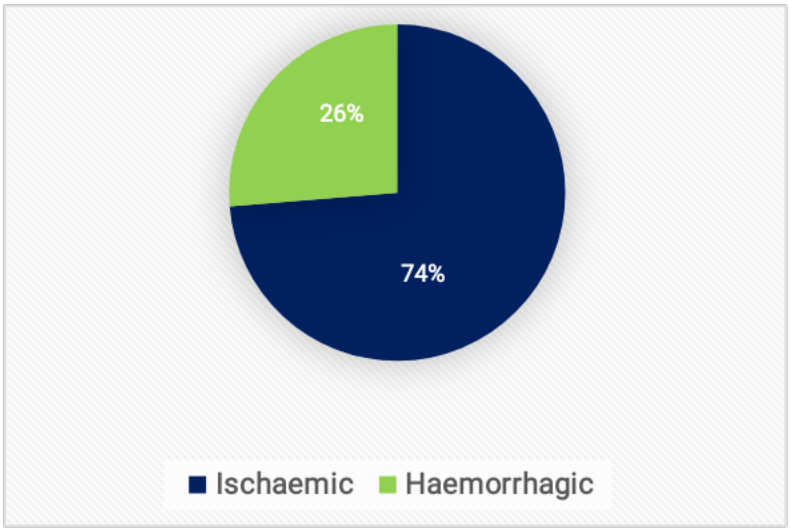

Figure 4.5: Stroke classification based on type among 346 cohorts Treated at Three Selected Hospitals in South Western Nigeria for a period of two years

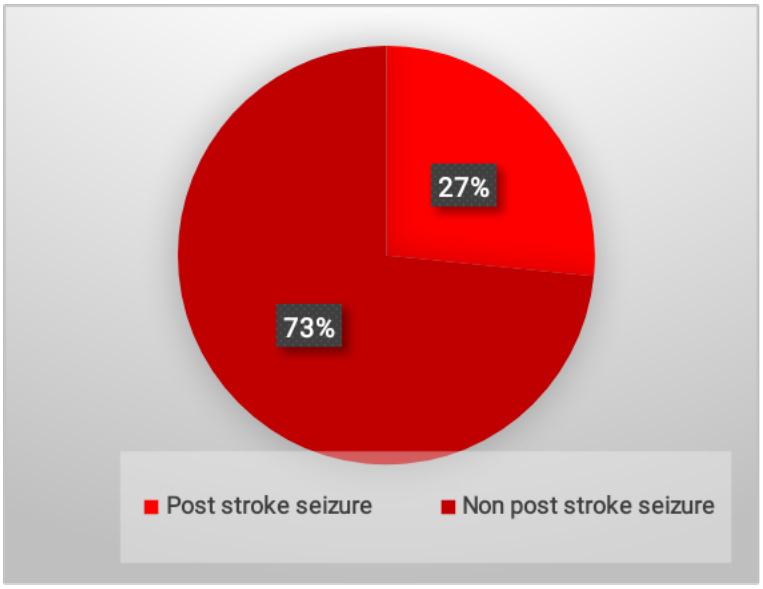

Figure 4.6: Stroke classification based on Seizure Occurrence/presence of Seizure among 92 Post-Stroke Seizure and 254 NSIS Patients Treated at Three Selected Hospitals in South Western Nigeria for a period of two years

NSIS – Non-Stroke Induced Seizure

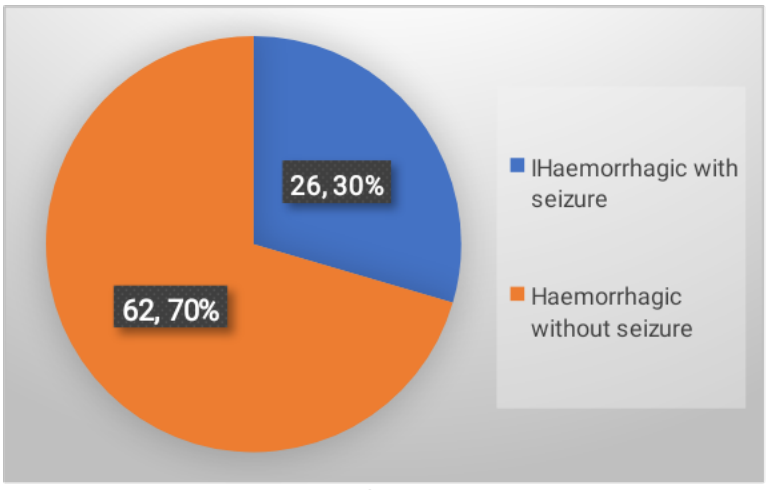

Figure 4.7: The Frequency of Haemorrhagic Stroke Participants with Stroke Induced Seizure and Non-Stroke Induced Seizure Treated at Three Selected Hospitals in South Western Nigeria for a period of two years

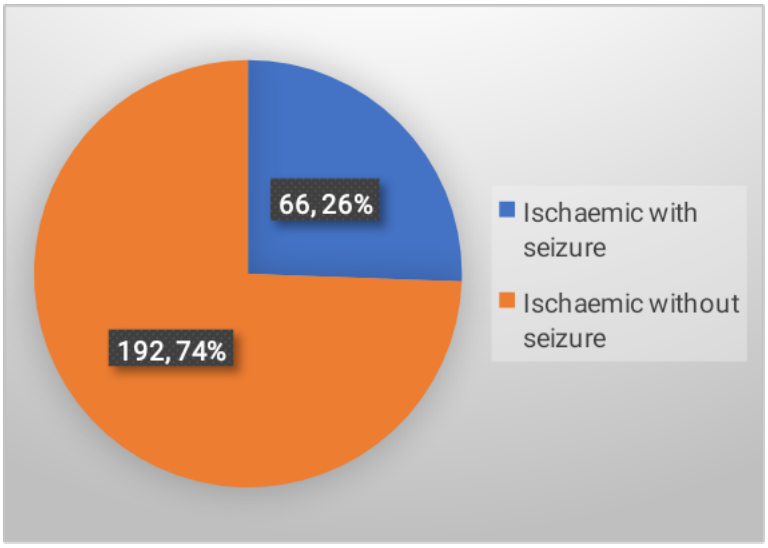

Figure 4.8: The Frequency of Ischaemic Stroke Participants with Stroke Induced Seizure and Non-Stroke Induced Seizure Treated at Three Selected Hospitals in South Western Nigeria for a period of two years

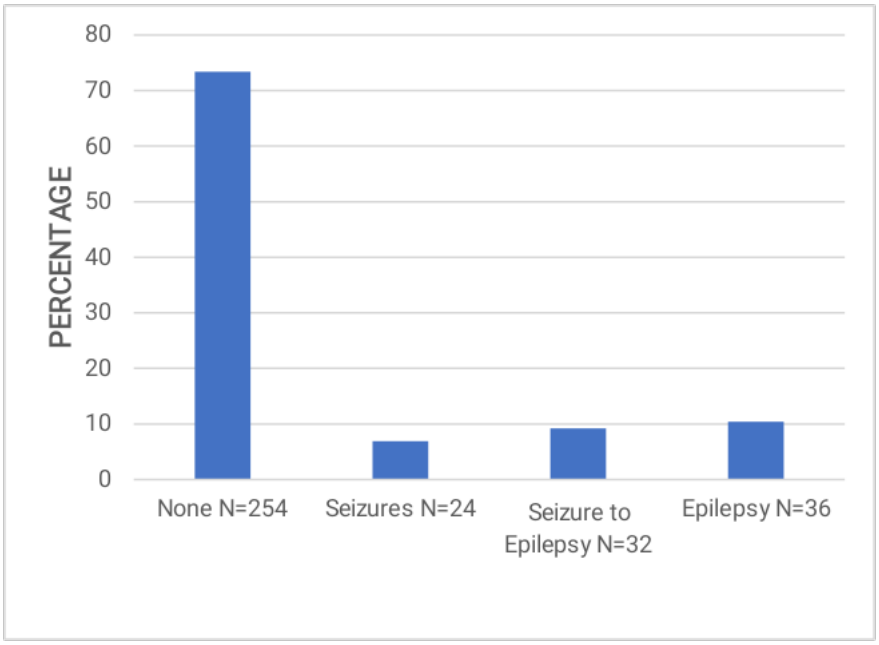

Figure 4.9: Frequency of Seizure and Epilepsy among Stroke Patients Treated at Three Selected Hospitals in South Western Nigeria for a period of two years.

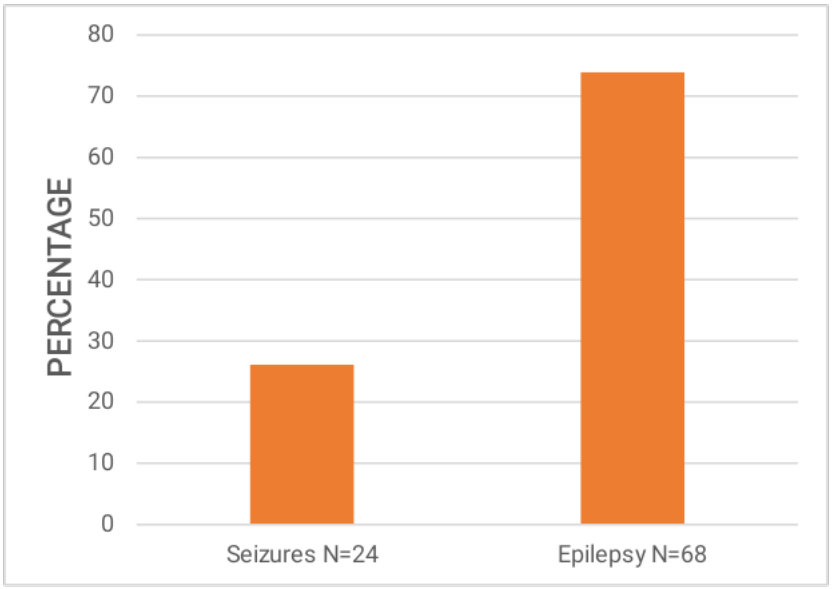

Figure 4.10: Frequency of Seizure and Epilepsy among 346 Stroke Patients Treated at Three Selected Hospitals in South Western Nigeria for a period of two years.

4.7: Comparison of Clinical characteristics of Stroke Survivors with or without Seizure Treated at Three Selected Hospitals in South Western Nigeria for a period of two years

Patterns of stroke location reveal that there were higher number of participants with ischemic stroke at frontal lobe [112(43.4%) vs 12(13.6%); p<0.001], parietal lobe [138(53.5%) vs 9(10.2%); p<0.001], temporal lobe [43(16.7%) vs 4(4.5%); p≤0.004], internal capsule [21(8.2%) vs 15(17.4%); p0.016], and lower number of participants at thalamus [16(6.2%) vs 33(37.5%); p<0.001] respectively compared to haemorrhagic stroke.

Among participants with ACA stroke, 60(23.3%) were ischaemic while 10(11.4%) were haemorrhagic stroke (p0.016). Majority of the participants had stroke in MCA region with 169(65.5%) as ischaemic and 37(42%) as haemorrhagic (p<0.001). In PCA region, 12(31%) were ischaemic and 42(47.7%) were haemorrhagic stroke (p<0.001).

The use of antihypertensives was seen among 196(76.0%) ischaemic stroke cohort and 78(88.6%) among haemorrhagic stroke cohort and this was statistically significant (p≤0.011). The median stroke size was 5.84(1-40) among ischaemic stroke cohort and 10.68(2-40) among haemorrhagic stroke cohort which is statistically significant (p<0.001) (See Table 4.5).

Table 4.5: Comparison of Clinical characteristics among 346 Participants with Ischaemic and Haemorrhagic Treated at Three Selected Hospitals in South Western Nigeria for a period of two years

Variables	Ischaemic n= 258	Haemorrhagic n = 88	Total N=346	x^2 Value	p Value
A. Clinical Characteristics					
Gender n (%) Male Female	 146(56.6) 112(43.4)	 53(60.2) 35(39.8)	 199(57.5) 147(42.5)	x^2=0.355	0.551
NIHSS at Presentation Mean (SD)	16.63±9.045)	18.61±8.848)	17.13±9.025)	F=3.197	0.075
Stroke Severity n (%) No stroke Minor stroke Moderate stroke Moderate to severe Severe stroke	 2(0.8) 26(10.7) 90(37.2) 47(19.4) 77(31.8)	 1(1.2) 2(2.3) 34(39.5) 17(19.8) 32(37.2)	 3(0.9) 28(8.5) 124(37.8) 64(19.5) 109(33.2)	x^2=5.997	0.199
Stroke size median (range)	5.84(1-40)	10.67(2-40)	7.073(1-40)	F=33.748	<0.001*
Hypertensive n(%) Anti-hypertensive n(%)	168(65.9) 196(76.0)	67(76.1) 78(88.6)		3.189 6.390	0.074 0.011*
Diabetics n(%) Anti-diabetics n(%)	57(22.4) 32(12.5)	11(12.5) 5(5.7)		3.996 3.138	0.046 0.077
Statin n(%)	102(39.5)	16(18.2)		13.313	<0.001*
Mass effect n(%)	16(6.2)	59(67.0)		143.081	<0.001*
Large artery	75(29.4)	2(100.0)		4.712	0.030*

atherosclerosis n(%)					
Raised ICP n(%)	45(17.6)	30(34.1)		10.354	0.001*
Aspiration pneumonia n(%)	36(14.1)	14(15.9)		0.169	0.681
PTE n(%)	9(3.5)	3(3.4)		0.003	0.958
B. Location					
Basal ganglia n(%) Caudate Lentiform	 8(3.1) 16(6.2)	 5(5.7) 25(28.4)	 13(3.8) 41(11.8)	 1.193 30.981	 0.275 <0.001 *
Lobar Involvement n(%) Frontal Lobe Parietal Lobe Temporal Lobe Occipital Lobe	 112(43.4) 138(53.5) 43(16.7) 19(7.4)	 12(13.6) 9(10.2) 4(4.5) 10(11.4)	 124(35.8) 147(42.5) 47(13.6) 29(8.4)	 25.298 50.258 8.273 1.367	 <0.001 * <0.001 * 0.004* 0.242
Subcortical n(%) Internal Capsule Thalamus	 21(8.2) 16(6.2)	 15(17.4) 33(37.5)	 36(10.5) 49(14.2)	 5.834 52.878	 0.016* <0.001 *
Infratentorial n(%) Cerebellum Brain stem Pons Midbrain	 12(4.7) 12(4.7) 10(3.9)	 4(4.5) 1(1.1) 1(1.1)	 16(4.7) 13(3.8) 11(3.2)	 0.005 2.242 1.600	 0.945 0.134 0.206
Cortical Involvement n(%) Cortical No cortical	 58(22.5) 200(77.5)	 13(14.8) 75(85.2)	 71(20.5) 275(79.5)	 2.390	 0.122

Age grouped <35 36-70 71-95	 8(3.1) 188(72.9) 62(24.0)	 2(2.3) 75(85.2) 11(12.5)	 10(2.9) 263(76.0) 73(21.1)	 x^2=5.610	 0.061
C. Arterial Territory					
ACA n(%) MCA n(%) PCA n(%)	60(23.3) 169(65.5) 31(12.0)	10(11.4) 37(42.0) 42(47.7)		5.750 14.989 50.271	0.016* <0.001 * <0.001 *

NIHSS – National Institute of Health Stroke Scale Score PTE: Pulmonary Thromboembolism, ICP: Intracranial Pressure, ACA: Anterior Cerebral Artery, MCA: Middle Cerebral Artery, PCA: Posterior Cerebral Artery, *p<0.05 comparing ischaemic and haemorrhagic

4.8: Mortality Rate Among 346 Participants Treated at Three Selected Hospitals in South Western Nigeria for a period of two years

The mortality rate among stroke cohort was 8.7%, 23.7%, 35.0%, 38.4% at 7days, 1month, 12 months and 24 months, respectively. Furthermore, mortality rate was higher among haemorrhagic stroke cohort compared to ischaemic stroke cohort from 7days to 24months and these were consistently statistically significant (See Table 4.6).

Table 4.6: Mortality Rate Among 346 Participants Treated at Three Selected Hospitals in South Western Nigeria for a period of two years

Variables	7days	1months	3months	6months	12months	24months
Stroke Patient n(%)	30(8.7)	82(23.7)	96(27.7)	118(34.1)	121(35.0)	133(38.4)
Ischaemic n(%)	18(7.0)	55(21.3)	63(24.4)	78(30.2)	80(31.0)	92(35.7)
Haemorrhagic n(%)	12(13.6)	27(30.7)	33(37.5)	40(45.5)	41(46.6)	41(46.6)
SIS n(%)	9(9.8)	24(26.1)	25(27.2)	29(31.5)	29(31.5)	32(34.8)
Seizure type						
ISPWS n(%)	2(3.0)	13(19.7)	13(19.7)	15(22.7)	15(22.7)	18(27.3)
HSPWS n(%)	7(26.9)	11(42.3)	12(46.2)	14(53.8)	14(53.8)	14(53.8)

SIS – Stroke Induced Seizures ISCH- Ischaemic Stroke Patients with Seizures HSPWS Haemorrhagic Stroke Patients with Seizures

4.9: Comparison of Sociodemographic Clinical Characteristics among 66 Ischaemic Stroke Patients and 26 Haemorrhagic Stroke Patients with Stroke Induced Epilepsy

Among the 92 participants that developed SIE, 54(58.7%) were males and 38(41.3%) were females. There were 66(26%) ischaemic and 26(29.5%) haemorrhagic stroke participant that developed SIE. The mean age of participants with SIE among ischaemic stroke patients is 62.14±14.43 compared to a value of 53.38±12.39 among haemorrhagic stroke patient with SIE and this attained a significant level (p≤0.008). The mean stroke volume among participants with ischaemic stroke with SIE is 11.14(39.50) compared to value of 29.43(37.00) among those with haemorrhagic stroke with SIE and this was significant (p<0.001).

Of the 62(67%) with MCA stroke with SIE, majority 50(75.8%) were ischaemic compared to 12(46.2%) of haemorrhagic stroke patients which was statistically significant (p≤0.006). Among those with PCA stroke, with SIE, 3(4.5%) were ischaemic compared to 11(42.3%) that had haemorrhagic stroke and this was significant (p<0.001). Among the 92 patients with SIE, the frequency of statins usage was 34(51.5%) among ischemic cohorts compared to 7(26.9%) among haemorrhagic stroke patients and this was significant (p≤0.033).

Furthermore, the presence of mass effect was more in the haemorrhagic cohorts 15(57.7%) compared to 5(7.6%) among ischaemic cohorts (p0.001) (See Table 4.7).

Table 4.7: Comparison of Sociodemographic and Clinical Characteristics of 66 Ischaemic Stroke Patients and 26 Haemorrhagic Stroke Patients with Stroke Induced Epilepsy

Variables	ISPWS n=66	HMPWS n=26	x^2 value	p value
Gender n(%) Male Female	 38(57.6) 28(42.4)	 16(61.5) 10(38.5)	0.121	0.728
Age Mean (SD)	62.14±14.43)	53.38±12.39)	T=2.721	0.008*
Stroke size Median (Range)	4.23(29.00)	10.75(28.00)	T=-2.819	0.006*
Stroke volume cm^3 Median (Range)	11.14(39.50)	29.43(37.00)	T=-4.605	<0.001*
Cortical involvement n(%) Cortical No cortical	 23(34.8) 43(65.2)	 10(38.5) 16(61.5)	0.106	0.7445
Hypertensive n(%)	43(68.3)	19(73.1)	0.203	0.653
Diabetics n(%)	26(41.3)	5(19.2)	3.938	0.047*
ACA n(%)	13(19.7)	4(15.4)	0.230	0.631
MCA n(%)	50(75.8)	12(46.2)	7.438	0.006*
PCA n(%)	3(4.5)	11(42.3)	20.616	<0.001*
Antihypertensive n(%)	49(74.2)	23(88.5)	2.217	0.137
Anti-diabetics n(%)	14(21.2)	3(11.5)	1.159	0.282
Statin n(%)	34(51.5)	7(26.9)	4.566	0.033*
Mass effect n(%)	5(7.6)	15(57.7)	27.536	<0.001*
Large artery atherosclerosis n(%)	16(25.4)	2(100.0)	5.388	0.020*

ACA: Anterior Cerebral Artery, MCA: Middle Cerebral Artery, PCA: Posterior Cerebral Artery, PTE: Pulmonary Thromboembolism, UTI: Urinary Tract

Infection, ICP: Intracranial Pressure, ISPWS: Ischaemic Stroke Patients with Seizures, HSPWS: Haemorrhagic Stroke Patients with Seizures, *p<0.05 comparing ISPWS and HMPWS.

4.10: Demographic, Clinical and Radio-imaging patterns among 92 Patients with Stroke Induced Seizure and Stroke Induced Epilepsy treated at Three Selected Hospitals South Western Nigeria over a period of two years

Of the 92(27%) with SIS/SIE, 24(26%) had seizure only, 32(35%) had seizures that progress to epilepsy and 36(39%) had epilepsy only after stroke. The M:F ratio among the different sub-groups (0.7:1) seizure only group, (1:1) seizure to epilepsy and (3.5:1) epilepsy only respectively.

There were higher mean NIHSS score, [25.54±12.42) vs 15.8±8.26); p<0.001], higher median size [11.54(9.60) vs 5.87(5.37); p≤0.005], and higher volume of lesion [24.27(14.26) vs 14.04(13.30); p≤0.006], higher mass effect [8(33.3%) vs 4(11.1%); p≤0.035], higher frequency of hypertension [21(100%) vs 21(58.3%) p≤0.001], higher frequency of diabetes [12(57.1%) vs 9(25%); p≤0.015] among seizure group compared to epilepsy. There was a statistically significant higher mean NIHSS [25.54±12.42) vs 15.81±8.76); p≤0.001] and higher frequency of hypertension [21(100%) vs 20(62.5%); p≤0.001] in the seizure group compared to seizure-epilepsy group. However, there was no statistically significant difference in the mean NIHSS, median size and volume of lesion values between the seizure-epilepsy and epilepsy only group.

Consistently the MR was higher in the seizure group compared to epilepsy group at 1month [17(70.8%) vs1(2.8%); p≤0.000] and 12months [18(75.1%) vs (2.8%); p≤0.000]. Similarly, MR was higher in seizure group compared to seizure to epilepsy groups at 1month [17(70.8%) vs 13(40%); p≤0.000] and 12months [17(70.8%) vs 1(2.8%); p≤0.010] (See Table 4.8).

Table 4.8: Demographics, Clinical and Radio-imaging patterns among 92 Patients with SIS/SIE Treated Three Selected Hospital in South Western, Nigeria over a period of two years

Variables	Seizure	Seizure-epilepsy	Epilepsy	p1-value	p2-value	p3-value
Gender n(%)						
Male	10(41.7)	16(50.0)	28(77.8)	0.004*	0.536	0.017*
Female	14(58.3)	16(50.0)	8(22.2)			
Age Mean(SD)	63.04±13.48)	59.31±12.60)	57.72±16.29)	0.190	0.292	0.657
NIHSS	25.54±12.42)	15.81±8.76)	15.22±7.27)	<0.001*	0.001*	0.762
Stroke size	11.54(9.66)	7.66(5.41)	5.87(5.37)	0.005*	0.061	0.176
Stroke volume	24.29(14.26)	19.47(13.81)	14.04(13.30)	0.006*	0.208	0.104
Mass effect	8(33.3)	8(25.0)	4(11.1)	0.035*	0.495	0.134
Ventricular effacement	5(20.8)	3(9.4)	3(8.8)	0.191	0.225	0.938
Raised ICP	6(28.6)	6(18.8)	6(16.7)	0.288	0.403	0.822
Hypertension	21(100.0)	20(62.5)	21(58.3)	0.001*	0.001*	0.726
Diabetes mellitus	12(57.1)	10(31.2)	9(25.0)	0.015*	0.061	0.566
Sleep disorder	0(0.0)	3(9.4)	3(8.3)	0.174	0.149	0.880
Cortical involvement						
Cortical	7(29.2)	14(43.8)	12(33.3)	0.734	0.265	0.378
Not cortical	17(70.8)	18(56.2)	24(66.7)			
Circulation						
ACA	5(20.8)	9(28.1)	3(8.3)	0.163	0.533	0.033*
MCA	14(58.3)	20(62.5)	28(77.8)	0.107	0.752	0.168
PCA	5(20.8)	4(12.5)	5(13.9)	0.480	0.401	0.866

Mortality 1 month	17(70.8)	6(18.8)	1(2.8)	<0.001*	<0.001*	0.031*
Mortality 3 months	17(70.8)	7(21.9)	1(2.8)	<0.001*	<0.001*	0.015*
Mortality 6months	18(75.0)	10(31.2)	1(2.8)	<0.001*	0.001*	0.001*
Mortality 12months	18(75.0)	10(31.2)	1(2.8)	<0.001*	0.001*	0.001*
Mortality 24months	18(75.0)	13(40.6)	1(2.8)	<0.001*	0.010*	<0.001*

*p<0.05 comparing either seizure and epilepsy, seizure and seizure-epilepsy, seizure-epilepsy and epilepsy, ICP- Intracranial Pressure, NIHSS- National Institute of Health Stroke Scale, ACA- Anterior Cerebral Artery, MCA- Middle Cerebral Artery, PCA- Posterior Cerebral Artery p1: seizures vs epilepsy, p2: seizures vs seizures to epilepsy, p3: seizures to epilepsy vs epilepsy

4.11: Trend of Background Wave Changes, Slowing pattern and Epileptiform pattern on EEG among 346 Stroke Patients and 92 Stroke Patients with Stroke Induced Epilepsy/Stroke Induced Seizure Treated at Three Selected Hospitals in South Western Nigeria over a period of two years

The section describes pattern of 2 separate EEG performed on 346 stroke patients at presentation and 12months. At presentation, among 258(74.6%) with ischemic stroke, the were 88(34.1%) Alpha, 107(41.5%) theta, 60(23.3%) delta and 3(1.2%) intermixed fast rhythm on EEG compared to 88(24.6%) haemorrhagic cohort with frequency of 20(22.7%) alpha, 36(40.9%) theta, 32(36.4%) delta and 0(0.0%) intermixed fast rhythm on EEG (p≤0.046). At 12months, the frequencies of background wave changes were comparable between the ischemic and haemorrhagic stroke cohorts (p≤0.440).

Furthermore, at presentation, 121(47.1%) of the 258(75%) ischaemic cohorts had presence of epileptiform pattern on EEG, compared to 38(43.2) of 88(24.6%) haemorrhagic cohort (p≤0.033). At 12months, among 258 ischaemic cohort, 64(38.5) had epileptiform pattern on EEG compared to 7(15.2%) among 88 participants with haemorrhagic stroke (p≤0.023). Among 92 participants with SIS/SIE, 53(80.3%) of the 66(72%) ischaemic group had epileptiform pattern at presentation compared to 19(73.1%) of 26(28%) haemorrhagic cohort (p≤0.032). Furthermore, at 12months, 32(71.2) of the ischaemic cohort had epileptiform pattern compared to 3(25.0) of 26 in the haemorrhagic (p≤0.022) (See Table 4.9).

Table 4.9: Trend of Background Wave Changes, Slowing pattern and Epileptiform pattern on EEG among 346 Stroke Patients and 92 Stroke Patients with Stroke Induced Epilepsy/Stroke Induced Seizure Treated at Three Selected Hospitals in South Western Nigeria over a period of two years

EEG	ISCH n(%)	HMG n(%)	x^2 value	p-value	ISPWS n(%)	HSPWS n(%)	x^2 value	p value
Background At presentation Alpha Theta Delta Intermixed fast	 88(34.1) 107(41.5) 60(23.3) 3(1.2)	 20(22.7) 36(40.9) 32(36.4) 0(0.0)	7.991	0.046*	 14(21.2) 31(47.0) 20(30.3) 1(1.5)	 4(15.4) 13(50.0) 9(34.6) 0(0.0)	0.864	0.834
Background At 12months Alpha Theta Delta Intermixed fast Intermixed slow	 118(70.2) 33(19.6) 11(6.5) 4(2.4) 2(1.2)	 37(82.2) 5(11.1) 3(6.7) 0(0.0) 0(0.0)	3.757	0.440	 33(66.0) 11(22.0) 4(8.0) 1(2.0) 1(2.0)	 11(91.7) 0(0.0) 1(8.3) 0(0.0) 0(0.0)	4.020	0.403
Slowing At presentation Focal Generalized Intermittent None	 3(1.2) 69(26.7) 77(29.8) 109(42.2)	` 0(0.0) 34(28.6) 31(35.2) 23(26.1)	9.215	0.027*	 2(3.0) 23(3.8) 23(34.8) 18(27.3)	 0(0.0) 14(53.8) 6(23.1) 6(23.1)	3.408	0.333
Slowing At 12months Generalized Intermittent None	 23(13.5) 52(30.6) 95(55.9)	 4(8.5) 13(27.7) 30(63.8)	1.255	0.534	 10(20.4) 22(44.9) 17(34.7)	 2(15.4) 3(23.1) 8(61.5)	3.183	0.204

Epileptiform At presentation Focal Generalized Focal generalized None	18(7.0) 92(35.8) 11(4.3) 136(52.9)	1(1.1) 37(42.0) 0(0.00 50(56.8)	8.734	0.033*	9(13.6) 35(53.0) 9(13.6) 13(19.7)	0(0.0) 19(73.1) 0(0.0) 7(26.9)	8.816	0.032*
Epileptiform At 12months Focal Generalized Focal generalized None	14(8.4) 42(25.3) 8(4.8) 102(61.4)	1(2.2) 6(13.0) 0(0.0) 39(84.8)	9.551	0.023*	8(17.8) 17(37.8) 7(15.6) 13(28.9)	0(0.0) 3(25.0) 0(0.0) 9(75.0)	9.660	0.022*

ISPWS: Ischaemic Stroke Patients with Seizure, HSPWS: Haemorrhagic Stroke Patients with Seizures, ISCH: Ischaemic Patients, HMG: Haemorrhagic Patients, *p<0.05 comparing either ISCH and HMG, OR ISPWS and HSPWS.

4.12: Comparison of Functional outcome as measured by Modified Ranking Scale among 258 Ischaemic Stroke and 88 Haemorrhagic Stroke Patients Treated at Three Selected Hospitals in South Western Nigeria over a period of two year.

The frequency of participants with good outcome among ischemic cohort was 92(35.7%) compared to 19(21.6%) among haemorrhagic cohort (p≤0.015). However, from 1 month [154(59.7%) versus 61(69.0%); p≤0.108] to 24months [124(51.5%) versus 48(57.1%): p≤0.368] the outcome parameters were comparable among ischaemic and haemorrhagic cohorts (See Table 4.10).

Table 4.10: Comparison of Functional outcome as measured by Modified Ranking Scale among 258 Ischaemic Stroke and 88 Haemorrhagic Stroke Patients Treated at Three Selected Hospitals in South Western Nigeria over a period of two year.

MRS	ISCH n(%)	HMG n(%)	x^2 value	p-value
At 14days[1]	92(35.7)	19(21.6)	5.960	0.015*
At 1month[1]	104(40.3)	27(30.7)	2.586	0.108
At 3months[1]	114(44.2)	29(33.0)	3.414	0.065
At 6months[1]	121(46.9)	33(37.5)	2.347	0.126
At 9months[1]	128(49.6)	37(42.0)	1.506	0.220
At 12months[1]	139(53.9)	40(45.5)	1.864	0.172
At 24months[1]	117(48.5)	36(42.9)	0.810	0.368
At 14days[2]	166(64.3)	69(78.4)	5.960	0.015*
At 1month[2]	154(59.7)	61(69.3)	2.586	0.108
At 3months[2]	144(55.8)	59(67.0)	3.414	0.065
At 6months[2]	137(53.1)	55(62.5)	2.347	0.126
At 9months[2]	130(50.4)	51(58.0)	1.506	0.220
At 12months[2]	119(46.1)	48(54.5)	1.864	0.172
At 24months[2]	124(51.5)	48(57.1)	0.810	0.368

ISCH: Ischaemic Patients, HMG: Haemorrhagic Patients, [1]: Good Outcome, [2]: Poor Outcome, MRS: Modified Ranking Scale, *p<0.05 comparing ISCH and HMG

4.13: Comparison of Functional outcome as measured by Modified Ranking Scale among 66 Ischaemic Stroke and 26 Haemorrhagic Stroke Patients with Stroke induced Epilepsy Three Selected Hospitals in South Western Nigeria over a period two years.

Furthermore, from day 14 [39(59.1%) versus 20(76.9%); p≤0.108] to 24months [29(47.5%) versus 16(64.0); p≤0.165], there were no differences in the MRS of participant with SIE who had ischaemic stroke and those with haemorrhagic stroke (See Table 4.11).

Table 4.11: Comparison of Functional outcome as measured by Modified Ranking Scale among 66 Ischaemic Stroke and 26 Haemorrhagic Stroke Patients with Stroke induced Epilepsy Three Selected Hospitals in South Western Nigeria over a period two years

MRS	ISPWS N(%)	HSPWS N(%)	x^2 value	p value
At 14days[1]	27(40.9)	6(23.1)	2.578	0.108
At 1month[1]	30(45.5)	8(30.8)	1.659	0.198
At 3months[1]	34(51.5)	9(34.6)	2.140	0.144
At 6months[1]	35(53.0)	9(34.6)	2.535	0.111
At 9months[1]	34(51.5)	10(38.5)	1.274	0.259
At 12months[1]	38(57.6)	10(38.5)	2.731	0.098
At 24months[1]	32(52.5)	9(36.0)	1.926	0.165
At 14days[2]	39(59.1)	20(76.9)	2.578	0.108
At 1month[2]	36(54.5)	18(69.2)	1.659	0.198
At 3months[2]	32(48.5)	17(65.4)	2.140	0.144
At 6months[2]	31(47.0)	17(65.4)	2.535	0.111
At 9months[2]	32(48.5)	16(61.5)	1.274	0.259
At 12months[2]	28(42.4)	16(61.5)	2.731	0.098
At 24months[2]	29(47.5)	16(64.0)	1.926	0.165

ISPWS: Ischaemic Stroke Patients with Seizure, HSPWS: Haemorrhagic Stroke Patients with Seizures, [1]: Good Outcome, [2]: Poor Outcome, MRS: Modified Ranking Scale

4.14: Comparison of Stroke Severity among 346 stroke patients (258 Ischaemic Stroke Patients and 88 Haemorrhagic) Treated at Three Selected Hospitals in South Western Nigeria over a period of two years.

Among 346 stroke patients, at presentation, the mean NIHSS was 16.63±9.05 among ischaemic cohorts compared 18.61±8.85 among haemorrhagic cohorts which was comparable. (p≤0.075). The severity was also comparable at 1month. At 3months, the mean NIHSS was 17.46±15.72 among ischaemic cohorts compared to 21.52±16.62 among haemorrhagic cohorts (p≤0.040). At 12months, the mean NIHSS was 17.10±17.47 among ischaemic cohorts compared to 22.19±19.07 among haemorrhagic cohorts (p≤0.022) (see Table 4.12).

Table 4.12: Stroke Severity as measured by NIHSS among 346 Stroke Patients (258 Ischaemic and 88 Haemorrhagic) treated at three selected hospitals in southwest Nigeria over a period of two years.

NIHSS	Ischaemic (Mean±SD)	Haemorrhagic (Mean±SD)	T value	p-value
At presentation	16.63±9.05	18.61±8.85	-1.788	0.075
At 24 hours	16.63±9.23	18.45±9.15	-1.607	0.109
At 72 hours	16.26±9.57	17.85±9.49	-1.348	0.179
At 14 days	16.78±11.72	18.95±12.03	-1.493	0.136
At 21 days	17.03±12.63	19.61±13.38	-1.629	0.104
At 1month	17.44±14.79	20.73±15.63	-1.773	0.077
At 3months	17.46±15.72	21.52±16.65	-2.062	0.040*
At 6months	17.49±16.63	21.78±17.46	-2.064	0.040*
At 9months	17.21±17.29	22.56±18.34	-2.469	0.014*
At 12months	17.10±17.47	22.19±19.07	-2.305	0.022*
At 24months	20.19±18.16	23.04±19.10	-1.217	0.225

ISCH: Ischaemic Patients, HMG: Haemorrhagic Patients, NIHSS: National Institute Health Stroke Scale Score, *p<0.05 comparing ischaemic and haemorrhagic.

4.15: Comparison of Stroke Severity as measured by NIHSS among 346 Stroke Patients, and 92 (66 Ischaemic Stroke Patients and 26 Haemorrhagic) with Stroke Induced Epilepsy/Stroke Induced Stroke Treated at Three Selected Hospitals in South Western Nigeria over a period of two years.

Similarly, among stroke patient with SIE, consistent severe stroke was seen among ischaemic stroke cohort compared to haemorrhagic there was a consistent difference in severity from 3months till 12months. At 3months, the mean NIHSS of ischaemic stroke cohort was lower indicating reduced severity compared to haemorrhagic stroke cohort [14.89±14.90 versus 23.69±17.60; p≤0.017]. At 1year the mean NIHSS was lower indicating reduced severity among ischaemic stroke cohort compared to haemorrhagic stroke cohort [14.17±16.16 versus 24.46±19.48; p≤0.011] (See Table 4.13).

Table 4.13: Showing Stroke Severity as measured by NIHSS among 346 Stroke Patients, and 92 (66 Ischaemic Stroke Patients and 26 Haemorrhagic) with SIE/SIS treated at three selected hospitals in southwest Nigeria over a period of two years

NIHSS	ISPWS (MEAN±SD)	HSPWS (MEAN±SD)	T value	p value
At presentation	17.74±10.07	19.08±10.85	-0.560	0.577
At 24 hours	17.32±10.09	18.42±11.26	-0.458	0.648
At 72 hours	16.41±10.28	17.42±11.75	-0.409	0.683
At 14 days	16.00±11.75	20.38±15.41	-1.470	0.683
At 21 days	16.30±13.12	20.00±15.77	-1.148	0.254
At 1month	16.06±14.47	22.73±17.20	-1.885	0.063
At 3months	14.89±14.90	23.69±17.60	-2.421	0.017*
At 6months	14.44±15.65	24.54±18.18	-2.661	0.009*
At 9months	14.33±16.65	24.73±19.20	-2.645	0.010*
At 12months	14.17±16.16	24.46±19.48	-2.593	0.011*
At 24months	18.25±17.39	25.04±19.65	-1.559	0.123

ISPWS: Ischaemic Stroke Patients with Seizure, HSPWS: Haemorrhagic Stroke Patients With Seizures, NIHSS: National Institute Health Stroke Scale Score, *p<0.05comparing ISPWS and HSPWS.

4.16: Comparison of Socio-biological Characteristics between Participants with Ischaemic Stroke with or without Seizure Treated at Three Selected Hospitals in South Western Nigeria over a period of two year.

Of the 258(75%) participants with ischaemic stroke, 66(26%) had SIS/SIE with 38(57.6%) males and 28(42.4%) females.

Twenty-six (41.3%) of individuals with ischaemic SIS/SIE had background DM whereas 31(16.1%) of ischaemic NSIE had DM ($p<0.001$). Again, 14(21.2%) of ischaemic SIS/SIE use antidiabetic while 18(9.4%) of ischaemic NSIE use antidiabetic ($p\leq0.012$). Concerning use of statin, 34(51.5%) of ischaemic SIS/SIE use statin while 68(38.4%) of ischaemic NSIE use statin ($p\leq0.021$). Again, presence of cortical involvement of cranial CT was higher 23(34.8%) in the ischaemic stroke patient with SIS/SIE compared to 35(18.2%) NSIE.

Furthermore, 13(19.7%) among Ischaemic cohorts with SIS/SIE had no epileptiform pattern compared to 123(64.4%) among NSIE which was significant ($p<0.001$). There was a significant difference between ischaemic cohort with SIE and NSIE with regards to sleep disorder ($p\leq0.016$), presence of stroke in MCA region (p0.030) and presence of slowing on EEG at presentation ($p\leq0.016$) (See Table 4.14, Table 4.15).

Table 4.14: Comparison of Socio-biological Characteristics between Participants with Ischaemic Stroke with or without Seizure Treated at Three Selected Hospitals in South Western Nigeria over a period of two year.

Variable n(%)	SIS/SIE n=66	NSIS n=192	Statistics	p-value
Gender Male Female	 38(57.6) 28(42.4)	 108(56.2) 84(43.8)	 0.035	 0.851
Mass effect	5(7.6)	11(5.7)	0.288	0.592
Antihypertensive	49(74.2)	147(76.6)	0.145	0.704
Anti-diabetics	14(21.2)	18(9.4)	6.253	0.012*
Statin	34(51.5)	68(35.4)	5.325	0.021*
Raised ICP	12(19.0)	33(17.2)	0.113	0.737
Aspiration pneumonia	5(7.9)	31(16.1)	2.637	0.104
PTE	4(6.3)	5(2.6)	1.954	0.162
UTI	6(9.5)	29(15.1)	1.247	0.264
Hypertension	43(68.3)	125(65.1)	0.209	0.647
Diabetes mellitus	26(41.3)	31(16.1)	17.251	<0.001*
Sleep disorder	4(6.3)	2(1.0)	5.816	0.016*
Cortical involvement Cortical Not cortical	 23(34.8) 43(65.2)	 35(18.2) 157(81.8)	 7.785	 0.005*
ACA n(%)	13(19.7)	47(24.5)	0.629	0.428
MCA n(%)	50(75.8)	119(62.0)	4.127	0.042*
PCA n(%)	3(4.5)	28(14.6)	4.681	0.030*
AGE Mean(SD)	62.14(14.43)	61.02(12.35)	0.608	0.543

NIHSS 0 n(%)	17.74(10.07)	16.24(8.66)	1.161	0.247
Stroke size	6.72(6.55)	5.54(6.65)	1.238	0.217
Stroke volume	14.73(13.59)	11.81(13.15)	1.546	0.123

SIS: Post Stroke Seizure Patients, NSIS: Non-Post Stroke Seizure Patients, ACA: Anterior Cerebral Artery, MCA: Middle Cerebral Artery, PCA: Posterior Cerebral Artery, IVH: Intraventricular Haemorrhage, NIHSS: National Institute Health Stroke Scale Score *$p<0.05$ comparing SIS/SIE and NSIS.

Table 4.15: Comparison of EEG characteristics between Individuals with Ischemic Stroke with or without Seizure Treated at Three Selected Hospitals in South Western Nigeria over a period of two years.

Variable n(%)	SIS/SIE n=66	NSIS n=192	Statistics	p-value
Background				
Alpha	14(21.2)	74(38.5)		
Theta	31(47.0)	76(39.6)	6.959	0.073
Delta	20(30.3)	40(20.8)		
Intermixed fast	1(1.5)	2(1.0)		
Epileptiform				
Focal	9(13.6)	9(4.7)		
Generalized	35(53.0)	57(29.8)	49.629	<0.001*
Focal -	9(13.6)	2(1.0)		
generalized	13(19.7)	123(64.4)		
No				
Slowing				
Focal	2(3.0)	1(0.5)	10.290	0.016*
Generalized	23(34.8)	46(24.0)		
Intermittent	23(34.8)	54(28.1)		
No	18(27.3)	91(47.4)		

SIS: Post Stroke Seizure Patients, NSIS: Non-Post Stroke Seizure Patients, *p<0.05 comparing SIS/SIE and NSIS

4.17: Comparison of Socio-biological Characteristics between participants with Haemorrhagic Stroke with or without Seizure Treated at Three Selected Hospitals in South Western Nigeria over a period of two years.

Of the 346 participants recruited, 88(24.5%) were haemorrhagic stroke. There were 53(60.2) males compared to 35(39.8%) females amounting to M:F ratio of 1.5:1. Furthermore 26(29.5%) of 88 haemorrhagic cohorts had SIE/SIS with 16(61.5%) males and 10(38.5%) females. There was presence of cortical involvement in 10(38.5%) haemorrhagic stroke patients with SIE/SIS compared to 3(4.8%) NSIS. Furthermore, 19(73.1%) haemorrhagic cohorts with SIE/SIS had epileptiform pattern compared to 19(30.6%) NSIS which was significant ($p \leq 0.001$) (See Table 4.16, Table 4.17).

Table 4.16: Comparison of Socio-biological Characteristics between Participants with Haemorrhagic Stroke with or without Seizure Treated at Three Selected Hospitals in South Western Nigeria over a period of two years.

Variable n(%)	SIE/SIS n=26	NSIS n=62	Statistics	p-value
Gender Male Female	 16(61.5) 10(38.5)	 37(59.7) 25(40.3)	 0.026	 0.871
Mass effect	15(57.7)	44(71.0)	1.461	0.227
Antihypertensive	23(88.5)	55(88.7)	0.001	0.973
Anti-diabetics	3(11.5)	2(3.2)	2.362	0.124
Statin	7(26.9)	9(14.5)	1.896	0.169
Raised ICP	6(23.1)	24(38.7)	1.992	0.158
Aspiration pneumonia	3(11.5)	11(17.7)	0.527	0.468
PTE	1(3.8)	2(3.2)	0.021	0.884
UTI	0(0.0)	4(6.5)	1.757	0.185
Hypertension	19(73.1)	48(77.4)	0.190	0.663
Diabetes mellitus	5(19.2)	6(9.7)	1.529	0.216
Sleep disorder	2(7.7)	1(1.6)	2.056	0.152
Cortical involvement Cortical Not cortical	 10(38.5) 16(61.5)	 3(4.8) 59(95.2)	 16.448	 <0.001*
ACA	4(15.4)	6(9.7)	0.592	0.442
MCA	12(46.2)	25(40.3)	0.256	0.613
PCA	11(42.3)	31(50.0)	0.434	0.510
IVH	4(15.4)	18(29.0)	1.820	0.177
Age (Mean±SD)	53±12.39)	57.84±11.9	-1.580	0.118

		3)		
NIHSS 0	19.08(10.85)	18.42(7.95)	0.316	0.752
Stroke size	11.16(7.42)	10.48(6.94)	0.409	0.684
Stroke volume	28.42(10.63)	25.17(13.78)	1.076	0.285

SIS: Post Stroke Seizure Patients, NSIS: Non-Stroke Induced Seizures, ACA: Anterior Cerebral Artery, MCA: Middle Cerebral Artery, PCA: Posterior Cerebral Artery, IVH: Intraventricular Haemorrhage, NIHSS: National Institute Health Stroke Scale Score *p<0.05 comparing SIS/SIE and NSIS.

Table 4.17: Comparison of EEG Characteristics between participants with Haemorrhagic Stroke with or without Seizure Treated at Three Selected Hospitals in South Western Nigeria over a period of two-year.

Variable n(%)	SIE/SIS n=26	NSIS n=62	Statistics	p-value
Background 0				
Alpha	4(15.4)	16(25.8)	1.652	0.438
Theta	13(50.0)	23(37.1)		
Delta	9(34.6)	23(37.1)		
Epileptiform 0				
Present	19(73.1)	19(30.6)	14.676	0.001*
Absent	7(26.9)	43(69.4)		
Slowing 0				
Focal	-	-	3.888	0.143
Generalized	14(53.8)	20(32.3)		
Intermittent	6(23.1)	25(40.3)		
No	6(23.1)	17(27.4)		

SIS: Post Stroke Seizure, NSIS: Non-Stroke Induced Seizures *p<0.05 comparing SIE/SIS and NSIS 0: Reading at presentation

4.18: Comparison of Socio-biological Characteristics and Mortality Rate among 254 with Non Stroke Induced seizure and 92 Stroke Induced Epilepsy (24 Seizure only, 32 Seizure to Epilepsy and 36 Epilepsy only cohorts) Treated at Three Selected Hospitals in South Western, Nigeria over a period of two years

Of the 346 participants recruited, 254(73%) had NSIS while 92(27%) had SIS. Of the 92(27%) with SIS, 24(26%) had seizure only, 32(35%) had seizures that progress to epilepsy and 36(39%) had epilepsy only after stroke. The M:F ratio among the different sub-group was (1.3:1) NSIS, (0.7:1) Seizure only, (1:1) seizure to epilepsy and (3.5:1) epilepsy only respectively.

There was a statistically significant lower mean NIHSS [16.78±8.53 vs 25.54±12.42; p≤0.000], lower mean size [4.28±39.00 vs 10.57±29.00; p≤0.002], mean volume of lesion [10.06±61.00 vs 28.50±39.00; p≤0.003] respectively in the NSIS compared to seizure only group. There was lower frequency of hypertension [173(68.5%) vs 21(100%); p≤0.002] and diabetes mellitus [37(14.6%) vs 12(57.1%) p<0.001] in the NSIS group compared to seizure only group. The clinical characteristics were comparable between the NSIS and epilepsy only group except for higher frequency of participant with Diabetes Mellitus [37(14.6%) vs 9(25%) p≤0.001] and lower frequency of sleep disorders [3(1.2%) vs 3(9.4%) p≤0.001] in the epilepsy group only. Consistently, MR was lower in the NSIS group compared to seizures only group at 1month [58(22.8%) vs17(70.8%) p<0.001] and 12monthss [92(36%) vs 18(75%), p≤0.000]. On the contrary, MR was higher in NSIS group compared to epilepsy only group at 1month [58(22.8%) vs 1(2.8%), p≤0.022] and 12months [92(36.2%) vs 1(2.8%) p≤0.002] (See Table 4.18).

Table 4.18: Comparison of Socio-biological Characteristics and Mortality Rate among 254 with Non Stroke Induced seizure and 92 Stroke Induced Epilepsy (24 Seizure only, 32 Seizure to Epilepsy and 36 Epilepsy only cohorts) Treated at Three Selected Hospitals in South Western, Nigeria over a period of two years

Variables n(%)	None N=254	Seizures N=24	Seizures to Epilepsy N=32	Epilepsy N=36	P_1 Value	P_2 Value	P_3 Value
Gender Male Female	 145(57.1) 109(42.9)	 10(41.7) 14(58.3)	 16(50.0) 16(50.0)	 28(77.8) 8(22.2)	0.026*	0.146	0.257
Stroke type Ischemic Hemorrhagic	 192(74.6) 62(24.4)	 15(62.5) 9(37.5)	 21(65.6) 11(34.4)	 30(83.3) 6(16.7)	0.188	0.160	0.920
Age (Mean±SD)	60.24±12.30	63.04±13.48	59.31±12.60	57.72±16.29	0.453	0.291	0.313
NIHSS 0, Mean(SD)	16.78±8.53	25.54±12.42	15.81±8.76	15.22±7.27	<0.001*	<0.001*	0.268
Size, Median(range)	4.28(39.00)	10.57(29.00)	6.67(23.00)	4.00(19.00)	0.009*	0.002*	0.966
Volume in cm^3 Median(range)	10.06(61.00)	28.50(39.00)	18.67(44.00)	13.63(39.50)	0.009*	0.003*	0.436
Mass effects	55(21.7)	8(33.3)	8(25.0)	4(11.1)	0.213	0.191	0.470
Ventricular effacement	25(9.8)	5(20.8)	3(9.4)	3(8.8)	0.392	0.097	0.854
Raised ICP	57(22.4)	6(28.6)	6(18.8)	6(16.7)	0.717	0.521	0.392
Hypertension	173(68.1)	21(100.0)	20(62.5)	21(58.3)	0.008*	0.002*	0.225
Diabetes	37(14.6)	12(57.1)	10(31.2)	9(25.0)	<0.001*	<0.001*	0.010*
Sleep disorder	3(1.2)	0(0.0)	3(9.4)	3(8.3)	0.005*	0.617	0.001*
1month mortality	58(22.8)	17(70.8)	6(18.8)	1(2.8)	<0.001*	<0.001*	0.022*
3months mortality	71(28.0)	17(70.8)	7(21.9)	1(2.8)	<0.001*	<0.001*	0.006*
6months mortality	89(35.0)	18(75.0)	10(31.2)	1(2.8)	<0.001*	<0.001*	0.003*
12months	92(36.2)	18(75.0)	10(31.2)	1(2.8)	<0.001*	<0.001*	0.002*

mortality							

ACA: Anterior Cerebral Artery, MCA: Middle Cerebral Artery, PCA: Posterior Cerebral Artery, IVH: Intraventricular Haemorrhage, NIHSS: National Institute Health Stroke Scale Score *p<0.05, p1: comparison of none, seizures, seizures to epilepsy and epilepsy, p2: none versus seizures only, p3: none versus epilepsy only.

4.19: Pattern of Mortality among 346 Stroke Patients Treated at Three Selected Hospitals over a period of two years

Of the 346 participants, 258(74.6%) had ischaemic stroke while 88(25.4) had haemorrhagic stroke. However, out of the 258 ischaemic stroke participants, 146(56.6%) were males and 112(43.4%) were females. Furthermore, of the 88 participants with haemorrhagic stroke, 53(60.2%) were males and 35(39.8%) are females. The mortality rate among stroke cohort was 8.7%, 23.7%, 35%, 38.4% at 7days, 1month, 12months and 24months, respectively. Furthermore, of the 88 individuals with haemorrhagic stroke, 13.6%, 30.7%, 46.6%, 46.6% respectively, died by 7days, 1month, 12month and 24months. On the other hand, 7.0%, 21.3%, 31.0%, 35.7% respectively died in the ischemic group. At 12months, there were higher M:F [14I(62.7%) vs 84(37.3%)], higher mean age [58.40±12.31 vs 63.21±13.27 p≤0.001], higher haemorrhagic deaths [ischaemic (178(79.1%) vs 80(66.1%), haemorrhagic 47(20.9%) vs 41(33.9%) p≤0.009], higher mean NIHSS±S.D at presentation [13.53±6.90 vs 23.83±8.70; p≤0.000], higher frequency of mass effect [34(15.1%) vs 41(33.9%); p<0.001] and large artery involvement [44(24.7%) vs 33(41.8%) p≤0.006] At 24months, there were higher M:F [alive 132(62.0%) vs 81(38.0%), dead 67(50.4%) vs 66(49.6.0%)], higher mean age [57.77±12.01 vs 63.80±13.27; p<0.001], higher mean NIHSS±S.D at presentation [13.46±6.86 vs 23.02±8.98; p<0.001], higher frequency of mass effect [32(15.0%) vs 43(32.3%); p<0.001] and large artery involvement [42(25.3%) vs35(38.5%) p≤0.028] among stroke patients that are dead compare those alive (See Table 4.19).

Furthermore, on computation of above factors that significantly associated with mortality (Age, gender, stroke severity, stroke size, mass effect, and large vessels involvement) into regression model, Age (Beta coefficient, 0.33, odd ratio 1.034 p 0.014, C.I 1.07-1.061) and NIHSS at presentation (Beta coefficient, 0.131, odd ratio 1.140 p≤0.000, C.I 1.093-1.189) were the only factors that attained significant level as determinants of mortality at 24months (See Table 4.20).

Table 4.19: Pattern of mortality among 346 Stroke Patients at 12months and 24months Treated at Three Selected Tertiary Hospitals for a period of two years

	12MONTHS				24MONTHS			
Variable n(%)	Alive	Dead	Statistics	p value	Alive	Dead	Statistic	p value
Gender Male Female	 141(62.7) 84(37.3)	 58(47.9) 63(52.1)	6.989	0.008*	 132(62.0) 81(38.0)	 67(50.4) 66(49.6)	4.506	0.034*
Age (Mean±SD)	58.40±12.35	63.21±13.27	-3.366	0.001*	57.77±12.04	63.80±13.32	-4.347	<0.001*
Hypertension	146(65.8)	89(73.6)	2.202	0.138	136(64.8)	99(74.4)	3.533	0.060
Diabetics mellitus	45(20.3)	23(19.0)	0.078	0.779	41(19.5)	27(20.3)	0.031	0.860
Hyperlipidemia	37(16.7)	20(16.7)	0.000	1.000	32(15.2)	25(18.9)	0.799	0.371
Chronic kidney Disease	3(1.4)	1(0.8)	0.187	0.665	3(1.4)	1(0.8)	0.324	0.570
Heart Disease	11(5.0)	7(5.8)	0.109	0.742	10(4.8)	8(6.0)	0.257	0.612
Stroke Type Ischaemic Haemorrhagic	 178(79.1) 47(20.9)	 80(66.1) 41(33.9)	7.007	0.009*	 166(77.9) 47(22.1)	 92(69.2) 41(30.8)	3.314	0.069
NIHSS 0, (Mean±SD)	13.53±6.90	23.83±8.70	-12.046	<0.001*	13.46±6.86	23.02±8.98	-11.166	<0.001*
ACA	46(20.4)	24(19.8)	0.018	0.893	41(19.2)	29(21.8)	0.331	0.565
MCA	140(62.2)	66(54.5)	1.925	0.165	135(63.4)	71(53.4)	3.397	0.065
PCA	41(18.2)	32(26.4)	3.197	0.074	39(18.3)	34(25.6)	2.588	0.108
Size, Median(range)	5.95(1-40)	9.17(1-40)	17.213	<0.001*	5.84(1-40)	9.04(1-40)	17.639	<0.001*
Mass Effect	34(15.1)	41(33.9)	16.334	<0.001*	32(15.0)	43(32.3)	14.446	<0.001*
Small Vessel Disease	39(21.9)	13(16.5)	1.009	0.315	35(21.1)	17(18.7)	0.210	0.647
Large Artery	44(24.7)	33(41.8)	7.583	0.006*	42(25.3)	35(38.5)	4.851	0.028*

*p<0.05, SD- Standard Deviation, NIHSS- National Institute of Health Stroke Scale, ACA- Anterior Cerebral Artery, MCA- Middle Cerebral Artery, PCA- Posterior Cerebral Artery, 0: Reading at presentation

Table 4.20: Predictors of Mortality among 346 Stroke Patients Treated at Three Selected Hospitals over a period of two years

Variables	B	p-value	Odds ratio	95% CI
Gender Male Female	 -0.222 Reference	0.489	0.801	0.426-1.503
Age (In Years)	0.033	0.014*	1.034	1.07-1.061
NIHSS at presentation	0.131	<0.001*	1.140	1.093-1.189
Stroke Size	0.040	0.123	1.041	0.989-1.189
Mass effect	0.724	0.342	2.062	0.464-9.170
Large Artery Atherosclerosis	0.509	0.127	1.664	0.866-3.196

*p<0.05, NIHSS- National Institute of Health Stroke Scale, CI- Confidence Interval

4.20: Predictors of Seizures and Epilepsy among 346 Stroke Patients Treated at Three Selected Hospitals in South Western Nigeria over a period of two years

On regression analysis, only DM (Beta coefficient -1.375, odd ratio 0.253, p≤0.020, C.I 0.08-0.804) and NIHSS at presentation (Beta coefficient 0.089, odd ratio 1.093. p≤0.010, C.I 1.021-1.170) predicted SIS. However, cortical involvement, (Beta coefficient -0842, odd ratio 2.321, p≤0.020, C.I 1.170- 4.603), sleep disorders (Beta coefficient 2.168, odd ratio 8,744. p≤0.009, C.I 0.08-0.804) and epileptiform pattern at presentation were the predictors of SIE (See Table 4.21).

Table 4.21: Predictors of Seizures and Epilepsy among 346 Stroke Patients Treated at Three Selected Hospitals in South Western Nigeria over a period of two year

Variables A	B	p-value	Odds ratio	95% CI
Diabetes mellitus	-1.375	0.020*	0.253	0.080-0.804
Hypertension	-18.534	0.997	0.000	0.000
Stroke size	0.028	0.595	1.028	0.927-1.141
Stroke volume	-0.002	0.939	0.998	0.940-1.059
NIHSS at presentation	0.089	0.010*	1.093	1.021-1.170
Background at presentation Alpha Delta Theta Intermixed	 16.860 15.306 14.601 Reference	 0.999 1.000 1.000	 0.000 0.000 0.000	 0.000 0.000 0.000
Slowing at presentation Focal Generalized Intermittent No	 38.739 1.466 0.321 Reference	 0.998 0.442 0.847	 6.672E+16 4.333 1.378	 0.000 0.103-182.575 0.053-36.017
Epileptiform at presentation Focal Generalized Focal-generalized No	 -33.519 1.496 -16.346 Reference	 0.998 0.162 0.999	 0.000 4.463 0.000	 0.000 0.549-36.262 0.000
VARIABLE B				
Diabetes	0.728	0.057	2.071	0.979-4.381
Cortical involvement Cortical Not cortical	 0.842 Reference	 0.016*	 2.321	 1.170-4.603
Sleep disorder	2.168	0.009*	8.744	1.730-44.202
Epileptiform at presentation Focal Generalized Focal-generalized No	 2.093 1.611 3.429 Reference	 <0.001* <0.001* <0.001*	 8.107 5.010 30.847	 2.653-24.769 2.477-10.131 5.7781 - 6.773
MCA	0.517	0.124	1.677	0.868-3.241

CI = Confidence Interval NIHSS = National Institute of Health Stroke Scale

*p<0.05 MCA=Middle Cerebral Artery A= seizure patients B= epilepsy

patients

4.21: Predictors of Seizures and Epilepsy among 258 Ischaemic and 88 Haemorrhagic Stroke Patients Treated at Three Selected Hospital in South Western Nigeria over a period of two year

Presence of DM, (Beta coefficient -1.461, p<0.001, odd ratio 0.232, C.I 0.108-0.500) sleep disorders (Beta coefficient -3.125, odd ratio 0.044, p≤0.020, C.I 0.04-0.489), use of statin (Beta coefficient -0.896, odd ratio 0.408, p<0.001, C.I 0.198-0.865) and epileptiform pattern at presentation (Beta coefficient -3.848, odd ratio 0.021, p<0.001, C.I 0.004-0.129) were the determinants of SIS among ischaemic stroke cohorts (See Table 4.2.13). However, cortical involvement (Beta coefficient -2.124, odd ratio 0.120, p≤0.005, C.I 2.027-0.527) was the only determinant among the haemorrhagic stroke patients (See Table 4.22).

Table 4.22: Predictors of Seizures and Epilepsy among 258 Ischaemic and 88 Haemorrhagic Stroke Patients Treated at Three Selected Hospital in South Western Nigeria over a period of two years

Variables	B	p-value	Odds ratio	95% CI
Diabetes mellitus	-1.461	<0.001*	0.232	0.108-0.500
Antidiabetics	.0.158	0.797	1.171	0.351-3.913
Statin	-0.896	0.019*	0.408	0.198-0.865
Cortical involvement Cortical Not cortical	 -0.619 Reference	 0.130	 0.538	 0.242-1.199
Sleep disorder	-3.125	0.011*	0.044	0.004-0.489
MCA	-0.581	0.180	0.560	0.239-1.309
PCA	1.499	0.117	4.479	0.687-29.185
Epileptiform at presentation Focal Generalized Focal-generalized No	 -2.190 -2.051 -3.848 Reference	 0.001* <0.001* <0.001*	 0.112 0.129 0.021	 0.031-0.406 0.047-0.350 0.004-0.129
Slowing at presentation Focal Generalized Intermittent No	 0.592 0.875 0.286 Reference	 0.679 0.131 0.560	 1.808 2.399 1.331	 0.110-29.751 0.769-7.482 0.509-3.481
Variable B				
Cortical involvement Cortical Not cortical	 Reference -2.124	 0.005*	 0.120	 0.027-0.527
Epileptiform at presentation Focal Generalized Focal-generalized No	 -20.761 -19.168 Reference	 1.000 1.000	 0.000 0.000	 0.000 0.000

CI = Confidence Interval *p<0.05 MCA=Middle Cerebral Artery

PCA=Posterior Cerebral Artery A=ischaemic post stroke patients

B=haemorrhagic post stroke patients

4.22: Trends of Cognitive pattern among 92 Post-Stroke Seizure And 254 Non Stoke Induced Seizure Patients Treated at Three Selected Hospital over a period of two years

Of the 264 stroke cohort who were assessed at 1month, 63(24%) had SIE and 201(76%) had NSIS. The overall mean CSID score at 1month was 47.46±19.68 in SIE group which was lower compared to 56.01±19.58 in NSIS group and this was statistically significant (p≤0.005). At 12months, the overall CSID score 55.66±18.47 was lower among SIS/SIE group compared to a mean score of 64.80±16.08 among NSIS group (p≤0.001). At 24months, of 213 patients left, 28.2(60) had SIE 71.8(153) had NSIS had NSIS. The overall mean CSID score was 56.27±18.32 in SIE group which was lower compared to a score of 65.88±14.78 in NSIE group (p≤0.001) (See Table 4.23, 4.24).

Table 4.23: Trends of Cognitive pattern among 92 Stroke Induced Epilepsy and 254 Non Stroke Induced Seizure Patients Treated at Three Selected Hospitals over a period of two years

Variables (Mean±SD)	1month		p-value	6months		p-value
	SIE n=63	NSIS n=196		SIS n=62	NSIS n=165	
Language						
Language naming	4.55±2.03	5.43±1.96	0.004*	5.03±1.70	5.91±1.70	0.001*
Expression definition	3.32±1.42	3.90±1.40	0.007*	3.61±1.22	4.24±1.22	0.002*
Expression repetition	0.53±0.74	0.74±0.41	0.001*	0.53±0.46	0.80±0.38	0.000*
Expression fluency	3.25±1.46	3.77±1.48	0.021*	3.61±1.30	4.05±1.30	0.036*
Expression total score	11.65±5.20	13.84±5.03	0.005*	13.96±10.30	15.06±4.44	0.282
Language	3.25±1.48	3.91± 1.40	0.002*	3.69±1.24	4.23±1.24	0.007*
compression	14.95±6.66	17.75±6.39	0.005*	16.45±5.80	19.31±5.66	0.002*
Total language score						
Memory						
Registration	2.42±1.12	2.99±1.16	0.001*	2.54±1.16	3.22±1.13	<0.001
Delayed recall	1.22±0.60	1.51±0.60	0.002*	1.30±0.58	1.61±0.58	*
Short test	3.78±1.90	4.46±1.84	0.016*	3.78±1.80	4.72±1.78	0.001*
Semantics	5.54±2.41	6.71±2.50	0.002*	5.63±2.67	7.18±2.54	0.001*
Total score	12.92±5.74	15.52±5.92	0.004*	13.31±6.14	16.66±6.00	<0.001
						*
						0.001*
Attention and						
calculation	4.81±2.51	5.61±2.43	0.033*	5.16±2.07	6.41±2.20	<0.001
Attention and	2.56±1.17	3.16±1.13	0.001*	2.82±1.08	3.41±1.00	*
calculation	3.87±1.72	4.73±1.68	0.001*	4.26±1.58	5.13±1.46	<0.001
Orientation time	6.44±2.89	7.90±2.80	0.001*	7.08±2.66	8.55±2.46	*
Orientation place						<0.001
Orientation total score						*
						<0.001
						*
Praxis assessment						

Square	1.94±0.81	2.26±0.90	0.015*	2.01±0.75	2.45±0.80	0.001*
Triangle with leg	1.90±0.83	2.24±0.92	0.014*	1.97±0.77	2.41±0.85	0.001*
Chevron	1.93±0.82	2.27±0.90	0.012*	2.01±0.75	2.44±0.81	0.001*
Rake	2.04±0.80	2.27±0.90	0.072	1.97±0.77	2.40±0.85	0.002*
Total score	8.20±3.10	9.20±3.47	0.058	7.96±3.01	9.72±3.26	0.001*
Overall score	47.46±19.68	56.01±19.58	0.005 *	50.49±17.74	60.66±18.40	0.001*

***p<0.05 comparing SIE/NSIS SIE – Stroke Induced Epilepsy NSIS – Non-Stroke Induced Seizure**

Table 4.24: Comparison of trends in Cognitive pattern among 92 Stroke Induced Epilepsy And 254 Non-Stroke Induced Seizure Patients Treated at Treated at Three Selected Hospitals over a period of two years

Variables	12months		p-value	24months		p-value
	SIE n =63	NSIS n= 160		SIE n = 60	NSIS n =153	
Language						
Language naming	5.44±1.78	6.26±1.46	0.001*	5.51±1.79	6.33±1.34	0.002*
Expression definition	3.92±1.18	4.48±1.00	0.001*	3.95±1.20	4.53±0.92	0.001*
Expression repetition	0.70±0.44	0.84±0.35	0.019*	0.73±0.43	0.84±0.35	0.099
Expression fluency	3.96±1.31	4.56±1.37	0.007*	4.02±1.33	4.56±0.98	0.005*
Expression total score	14.02±4.49	16.08±3.78	0.002*	14.22±4.49	16.26±3.48	0.003*
Language compression	3.90±1.38	4.46±1.13	0.004*	3.98±1.38	4.52±1.04	0.007*
Total language score	17.9±5.73	20.55±4.84	0.002*	18.22±5.73	20.79±4.43	0.003*
Memory						
Registration	2.90±1.23	3.40±1.08	0.006*	2.95±1.22	3.49±1.00	0.005*
Delayed recall	1.52±0.50	1.75±0.45	0.002*	1.54±0.50	1.79±0.41	0.001*
Short test	4.28±1.94	5.04±1.71	0.008*	4.37±1.91	5.18±1.58	0.007*
Semantics	6.38±2.87	7.68±2.41	0.002*	6.49±2.78	7.87±2.20	0.001*
Total score	15.28±6.23	17.93±5.45	0.004*	15.51±6.09	18.38±4.96	0.002*
Attention and calculation						
Attention and calculation	5.92±2.31	7.01±1.92	0.001*	5.76±2.36	7.13±1.75	0.000*
Orientation time	3.26±1.04	3.60±0.87	0.020*	3.34±1.04	3.66±0.79	

Orientation place Orientation total score	4.88±1.56 8.14±2.60	5.43±1.26 9.06±2.11	0.011* 0.012*	5.00±1.55 8.34±2.58	5.51±1.15 9.18±1.94	0.037* 0.022* 0.027*
Praxis assessment Square Triangle with leg Chevron Rake Total score	 2.12±0.86 2.04±0.91 2.12±0.86 2.04±0.91 8.32±3.51	 2.54±0.79 2.50±0.84 2.54±0.79 2.50±0.84 10.09±3.22	 0.001* 0.001* 0.001* 0.001* 0.001*	 2.10±0.88 2.05±0.91 2.10±0.88 2.05±0.91 8.29±3.57	 2.57±0.77 2.53±0.82 2.57±0.77 2.53±0.82 10.21±3.13	 0.001* 0.002* 0.001* 0.001* 0.001*
Overall score	55.66±18.47	64.80±16.08	0.001*	56.27±18.32	65.88±14.78	0.001*

***p<0.05 comparing SIE/NSIS SIE – Stroke Induced Epilepsy NSIS – Non-Stroke Induced Seizure**

4.23: Comparison of EEG Characteristics among 92 Stroke Induced Epilepsy/ Stroke Induced Seizure (46 Carbamazepine versus 46 Levetiracetam) Treated at Three Selected Hospitals in South Western Nigeria over a period of 2years

The frequency of alpha, theta, delta and intermixed were 6(13%), 23(50%), 16(34.8%), 1(1.2%) respectively in the CBZ compare to 12(26.1), 21(45,7), 13(28.3%), 0(0%) respectively in LEV group. This is however not statistically significant (p≤0.334). Similarly, at 12months, the frequency of alpha, theta, delta and intermixed fast and slow was 15(55.6%), 7(25.9%), 3(11.1%), 1(3.7%) and1(3.7%) in the CBZ group compared to respectively compared to 29(82.9%), 4(11.4%), 2(5.7%), 0(0%) and 0(0%) in the LEV group.

The frequency of fast and slow waves on EEG were comparable at

presentation, the frequency of fast wave was 17(60.7%) CBZ compared to 29(82.9%) LEV (p≤0.049) (See Table 4.25).

Table 4.25: EEG pattern among 92 Stroke Induced Epilepsy/ Stroke Induced Seizure (46 CBZ versus 46 LEV) Treated at Three Selected Hospitals in South Western Nigeria over a period of 2 years

Variable	CBZ N (%)	LEV N (%)	p value	Frequency	CBZ N (%)	LEV N (%)	p value
Background at Presentation Alpha Theta Delta Intermixed fast	6(13) 23(50) 16(34.8) 1(2.2)	12(26.1) 21(45.7) 13(28.3) 0(0)	0.334	Frequency Presentation Fast Slow	8(17.4) 38(82.6)	12(26.1) 34(73.9)	0.312
Background 6 months Alpha Theta Delta Intermixed fast Intermixed slow	12(41.4) 11(37.9) 4(13.8) 1(3.4) 1(3.4)	29(78.4) 6(16.2) 2(5.4) 0(0) 0(0)	0.035*	Frequency 6 months Fast Slow	14(46.7) 16(53.3)	26(70.3) 11(29.7)	0.050
Background 12months Alpha Theta Delta Intermixed fast Intermixed slow	15(55.6) 7(25.9) 3(11.1) 1(3.7) 1(3.7)	29(82.9) 4(11.4) 2(5.7) 0(0) 0(0)	0.162	Frequency 12months Fast Slow	17(60.7) 11(39.3)	29(82.9) 6(17.1)	0.049*
Epileptiform pattern at Presentation Focal Generalized Focal-generalized None	3(6.5) 30(65.2) 3(6.5) 10(21.7)	6(13) 24(52.2) 6(13) 13(21.7)	0.446	Slowing at Presentation Focal Generalized Intermittent None	2(4.3) 19(41.3) 17(37) 8(17.4)	0(0) 18(39.1) 12(26.1) 16(34.8)	0.135
Epileptiform pattern at 6 months Focal Generalized Focal-generalized None	3(10.7) 18(64.3) 1(3.6) 6(21.4)	6(16.2) 17(45.9) 6(16.2) 8(21.6)	0.294	Slowing at 6 months Focal Generalized Intermittent None	0(0) 7(23.3) 14(46.7) 9(30)	0(0) 7(18.9) 14(37.8) 16(43.2)	0.537
12month Focal Generalized Focal-generalized	2(8) 16(64) 1(4)	6(18.8) 4(12.5) 6(18.8)	0.001*	Slowing at 12months Focal Generalized	0(0) 5(18.5)	0(0) 7(20)	0.516

None	6(24)	16(50)		Intermittent None	13(48.1) 9(33.3)	12(34.3) 16(45.7)	

4.24 Socio-biological Characteristics of 92 Patients Treated with Levetiracetam or Carbamazepine at Three Selected Hospitals in South Western Nigeria over a period of one year

Of the 92 participants that developed SIS/SIE, 54(58.7%) were males and 38(41.3%) were females, amounting to a M:F ratio of 1.4 to 1 ($p<0.05$). The mean age of participants on LEV was 59.39±13.89 compared to the mean age of 59.98±15 of participants on LEV ($p\leq0.835$). The mean NIHSS at presentation were comparable at presentation in the two groups with a value of 17.83±10.80 in the CBZ group compared to a value of 18.41±9.78 in the LEV group ($p\leq0.785$). The mean NIHSS score at 24months was significantly higher in patients on (24.27±17.85) CBZ compared to those on (15.68±17.89) LEV ($p\leq0.034$). The socio-demographic, clinical characteristics, and MR of participant with seizures only that are on CBZ were statistically comparable to those on LEV except for NIHSS at 12months ($p\leq0.047$) and MR at 1month ($p\leq0.012$). The NIHSS mean score was lower in SIS group on (39.17±9.82) CBZ compared to those on (25.17±20.81) LEV.

The frequency of those with good outcome among those with SIS only on 5(41.7%) LEV was compared to none in the CBZ group. Furthermore, the socio-demographic, clinical and mortality characteristics of participants were comparable in the CBZ and LEV groups among the those with SIE and seizures that progress to epilepsy (See Table 4.26).

Table 4.26: Comparison of Socio-biological Characteristics of 92 Stroke Induced Epilepsy/Stroke Induced Seizure and 24 only Stroke Induced Seizure Patients Treated with Carbamazepine or Levetiracetam at Three Selected Hospitals in South Western Nigeria over a period of one year

Variables	CBZa	LEVa	p value	CBZb	LEVb	p value
Age Mean(SD)	59.98±15.00	59.35±13.89	0.835	64.42±14.64	61.67±12.72	0.628
Gender Male N(%) Female N(%)	 19(41.3) 27(58.7)	 35(76.1) 11(23.9)	0.010*	 3(25) 9(75)	 7(58.3) 5(41.7)	0.098
Volume median(range)	20.31(14.63)	16.89(13.68)	0.249	23.92(15.55)	24.67(13.52)	0.901
NIHSS at presentation	17.83±10.80	18.41±9.78	0.785	26.33±11.45	24.75±13.79	0.762
NIHSS at 1 month	20.85±16.11	15.04±14.45	0.072	36.33±13.26	26.83±18.75	0.166
NIHSS at 1 year	22.59±17.95	11.57±15.28	0.002*	39.17±9.82	25.17±20.81	0.047*
NIHSS at 1month Not severe Severe	 22(47.8) 24(52.2)	 36(78.3) 10(21.7)	0.002*	 2(16.7) 10(83.3)	 10(83.3) 2(16.7)	0.001*
NIHSS at 1year Not severe Severe	 21(45.7) 25(54.3)	 35(76.1) 11(23.9)	0.003*	 1(8.3) 11(91.7)	 5(41.7) 7(58.3)	0.059
MRS at 1 month Good outcome N(%) Poor outcome N(%)	 15(32.6) 31(67.4)	 23(50) 23(50)	0.090	 0(0) 12(100)	 5(41.7) 7(58.3)	0.012*
MRS at 1 year Good outcome N(%) Poor outcome N(%)	 19(41.3) 27(58.7)	 29(63) 17(37)	0.037*	 1(8.3) 11(91.7)	 5(41.7) 7(58.3)	0.059
Mortality at 1 month N(%)	15(32.6)	9(19.6)	0.154	10(83.3)	7(58.3)	0.178
Mortality at 1 year N(%)	20(43.5)	9(19.6)	0.014*	11(91.7)	7(58.3)	0.059
CSID AT 1month CI n(%) NCI n(%)	 42(91.3) 4(8.7)	 36(78.3) 10(21.7)	0.082	 12(100.0) 0(0.0)	 12(100.0) 0(0.0)	0.999
CSID at 1year CI n(%) NCI n(%)	 20(43.5) 6(13.0)	 16(34.8) 21(45.7)	0.008	 1(100.0) 0(0.0)	 0(0.0) 5(100.0)	0.014

*p<0.05 CBZa: all SIS/SIE on Carbamazepine LEVa: all SIS/SIE on Levetiracetam CBZb: only SIS patients on Carbamazepine LEVb: only SIS patients on Levetiracetam CI: Cognitively Impaired NCI: Not-cognitively Impaired

4.25: Outcomes of 92 Stroke-Induced Seizure disorder Treated with Carbamazepine or Levetiracetam at Three Selected Hospitals in South Western Nigeria over a period of two years

At 24months, the frequency of participants with good stroke outcome was lower in patients using 16(36.4%) CBZ compared to those on 25(59.5%) LEV ($p \leq 0.037$) The MR at 24months was higher in patients on 21(45.7%) CBZ compared to those on 11(23.9%) LEV (See Table 4.27).

Table 4.27: Socio-biological Characteristics of 92 Stroke Induced Epilepsy/Seizure and 24 only Stroke Induced Seizure Patients Treated with Carbamazepine or Levetiracetam at Three Selected Hospitals in South Western Nigeria over a period of two years

Variables	CBZa	LEVa	p value	CBZb	LEVb	p value
NIHSS at 2 years	24.27±17.85	15.68±17.89	0.034*	39.17±9.82	32.89±18.08	0.319
NIHSS at 2years Not severe Severe	 20(43.5) 26(56.5)	 33(71.7) 13(28.3)	0.006*	 1(8.3) 11(91.7)	 5(41.7) 7(58.3)	0.059
MRS at 2 years Good outcome N(%) Poor outcome N(%)	 16(36.4) 28(63.6)	 25(59.5) 17(40.5)	0.032*	 1(8.3) 11(91.7)	 5(41.7) 7(58.3)	0.059
Mortality at 2 years N(%)	21(45.7)	11(23.9)	0.029*	11(91.7)	7(58.3)	0.059
CSID at 2years CI NCI	 17(37.0) 6(13.0)	 6(13.0) 16(34.8)	0.002*	 1(100.0) 0(0.0)	 0(0.0) 2(100.0)	0.083

*p<0.05 CBZa: all SIS/SIE on Carbamazepine LEVa: all SIS/SIE on Levetiracetam CBZb: only SIS patients on Carbamazepine LEVb: only SIS patients on Levetiracetam CI: Cognitively Impaired NCI: Not-cognitively Impaired

4.26: Trend of Cognitive Function among 92 Stroke Induced Epilepsy/Seizure patients treated with Carbamazepine or Levetiracetam at Three Selected Hospitals in South Western Nigeria over a period of two years

Of the 92 patients that developed SIE/SIS had 46 each on CBZ or LEV respectively, at 1month, only 41 had developed SIS/SIE and were on AEDs, [21CBZ vs 20LEV] and the overall CSID score was 29.58±26.08 in CBZ group which was lower compared to 43.24±21.58 in the LEV group ($p \leq 0.007$).

At 6months, only 68 were on AEDs, [35CBZ vs 33LEV], the overall CSID score was 30.34±26.70 in CBZ group which was lower compared to 43.39±28.04 in LEV group ($p \leq 0.025$)

At 12months, only 60 were on AEDs, [30CBZ vs 30LEV]. The overall CSID score was 29.13±29.13 in CBZ group which was lower compared to 47.83±28.50 in LEV group ($p \leq 0.003$). Consistently, the overall CSID and its subdomain score was higher in the CBZ group compared to the LEV group from 1month to 12months (See Table 4.28).

Table 4.28: Trend of cognitive function among 92 Stroke Induced Epilepsy/Seizure on Carbamazepine and Levetiracetam Treated at Three Selected Hospitals in South Western Nigeria over a period of two years.

Variables 1 (Mean±SD)	1month		p-value	6months		P-value	12months		p-value
	CBZ n=20	LEV n=21		CBZ n=35	LEV n=33		CBZ n=26	LEV n=37	
Language									
Expression Naming	2.88(2.68)	4.20(2.10)	0.010*	3.12(2.76)	4.24(2.61)	0.049*	2.91(2.94)	4.65(2.65)	0.004*
Expression Definition	2.14(1.92)	3.00(1.54)	0.020*	2.27(1.98)	3.02(1.87)	0.065	2.16(2.10)	3.30(1.90)	0.007*
Expression Repetition	0.32(0.44)	0.41(0.43)	0.336	0.32(0.44)	0.46(0.48)	0.145	0.36(0.47)	0.57(0.49)	0.041*
Expression Fluency	2.01(1.87)	3.04(1.56)	0.005*	2.23(1.97)	3.07(1.91)	0.041*	2.11(2.14)	3.39(1.92)	0.003*
Expression Total Score	7.36(6.77)	10.65(5.52)	0.012*	9.22(12.47)	10.78(6.76)	0.456	7.53(7.53)	11.91(6.84)	0.005*
Language compression	2.05(1.91)	3.00(1.54)	0.011*	2.27(1.98)	3.11(1.92)	0.042*	2.10(2.14)	3.22(2.00)	0.011*
Total language score	9.48(8.72)	13.65(7.06)	0.013*	10.14(9.05)	13.94(8.65)	0.043*	9.64(9.65)	15.15(8.77)	0.005*
Memory									
Registration	1.46(1.35)	2.30(1.23)	0.002*	1.46(1.41)	2.22(1.63)	0.019*	1.44(1.57)	2.48(1.68)	0.003*
Delayed recall	0.76(0.71)	1.11(0.67)	0.018*	0.74(0.71)	1.17(0.80)	0.007*	0.80(0.79)	1.30(0.79)	0.003*
Short test	2.26(2.18)	3.59(1.96)	0.003*	2.15(2.12)	3.26(2.51)	0.024*	2.13(2.38)	3.61(2.60)	0.006*
Semantics	3.43(3.00)	5.35(2.68)	0.002*	3.32(3.26)	4.72(3.75)	0.059	3.24(3.59)	5.26(3.93)	0.012*
Total score	7.88(7.14)	12.26(6.35)	0.003*	7.64(7.50)	11.46(8.60)	0.026*	7.78(8.33)	12.72(8.88)	0.008*
Attention and calculation									
Attention and calculation	3.01(2.92)	4.09(2.45)	0.059	3.00(2.83)	4.61(3.01)	0.010*	3.02(3.20)	5.74(3.23)	<0.001
Orientation time	1.63(1.51)	2.30(1.23)	0.021*	1.72(1.57)	2.39(1.54)	0.041*	1.71(1.73)	2.74(1.58)	*
Orientation place	2.46(2.27)	3.50(1.80)	0.016*	2.59(2.34)	3.61(2.30)	0.037*	2.58(2.59)	4.09(2.37)	0.004*
Orientation total score	4.09(3.78)	5.80(3.02)	0.018*	4.30(3.92)	6.00(3.84)	0.039*	4.29(4.32)	6.83(3.96)	0.005*
									0.004*
Praxis assessment									
Square	1.18(1.07)	1.83(0.84)	0.002*	1.14(1.06)	1.90(1.11)	0.001*	1.09(1.14)	1.96(1.17)	0.001*
Triangle with leg	1.14(1.05)	1.83(0.84)	0.001*	1.10(1.04)	1.90(1.11)	0.001*	1.04(1.12)	1.78(1.22)	0.004*
Chevron	1.17(1.07)	1.83(0.84)	0.002*	1.14(1.06)	1.90(1.11)	0.001*	1.09(1.14)	1.96(1.17)	0.001*
Rake	1.22(1.09)	1.91(0.83)	0.001*	1.10(1.04)	1.90(1.11)	0.001*	1.04(1.12)	1.78(1.22)	0.004*
Total score	4.93(4.36)	7.78(3.26)	0.001*	4.48(4.18)	7.57(4.44)	0.001*	4.27(4.50)	7.48(4.72)	0.001*
Overall total score	29.58(26.08)	43.24(21.58)	0.007*	30.34(26.70)	43.39(28.04)	0.025*	29.13(29.13)	47.83(28.50)	0.003*

*p<0.05 comparing CBZ and LEV, LEV-Levetiracetam, CBZ-Carbamazepine, SD- Standard Deviation

4.27: Frequency of seizures among 160 stroke patients on prophylactic AEDs and 80 without prophylactic AEDs treated at three selected tertiary hospitals from January 2019 to June 2021

Of the 240 stroke patients recruited, 160 (67%) were on prophylactic AEDs while 80(33%) were not on prophylactic AEDs. Thirty-four (14.2%) of the 240 participants recruited into this phase developed SIS (See figure 4.11). Seventeen (10.6%) of the 160 stroke patients on prophylactic AEDs and 17(21.3%) of 80 stroke patients not on prophylactic AEDs respectively developed SIS (See Figure 4.12). Furthermore, among the 160 patients on prophylaxis, 10(12.5%) of those on CBZ and 7(8.8%) of those on LEV respectively developed SIS (See Figure 4.13).

Consistently, there were more participants with poor outcome among the no AED prophylactic group compare to AED prophylactic group at 1month [59(73.8%) vs 92(57.5%); p≤0.014], and 12months [47(58.8%) vs 59(36.9%); p≤0.001] (See Figure 4.14).

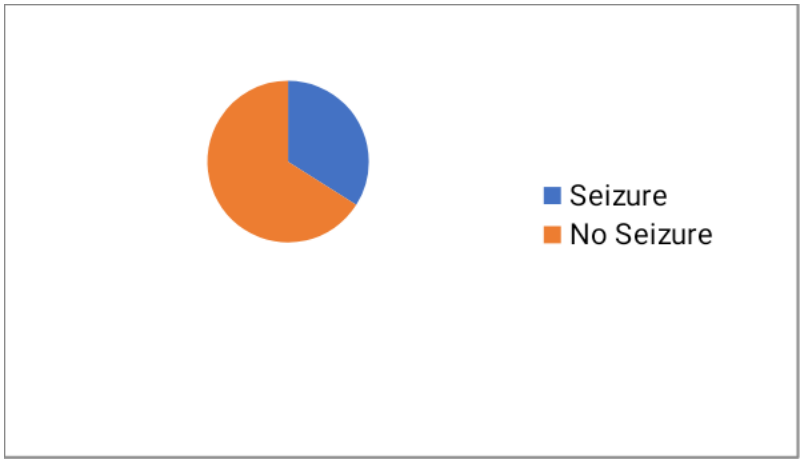

Figure 4.11: Frequency of Seizures among 240 Stroke Patients (prophylactic and non-prophylactic) Treated at Three Selected Tertiary hospitals from January 2019 to June 2021

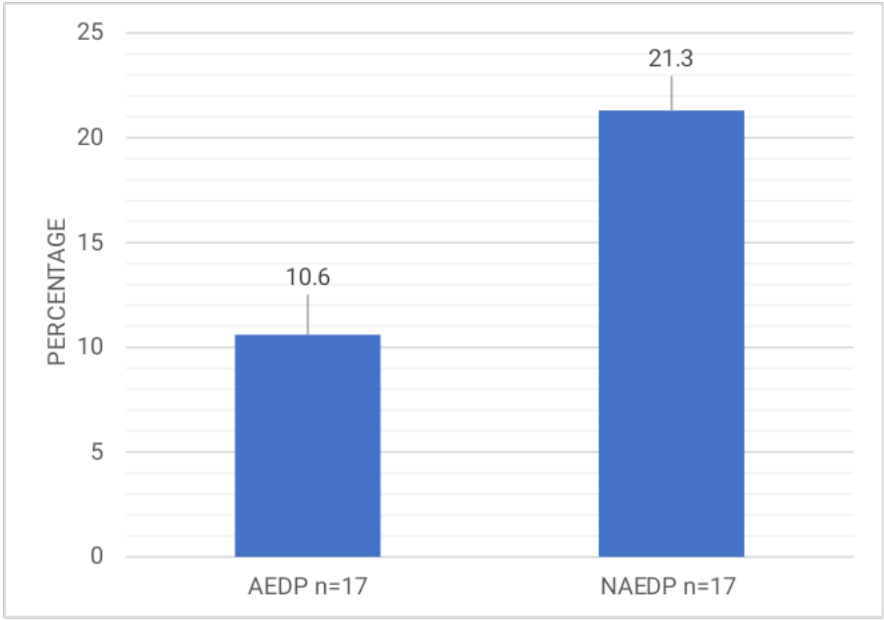

Figure 4.12: Frequency of development of Seizure among 160 Stroke Patients on AED and 80 Stroke Patients not on AED prophylaxis Treated at Three Selected Tertiary Hospitals from January 2019 to June 2021

AEDP=AED Prophylaxis, NAEDP=No AED Prophylaxis.

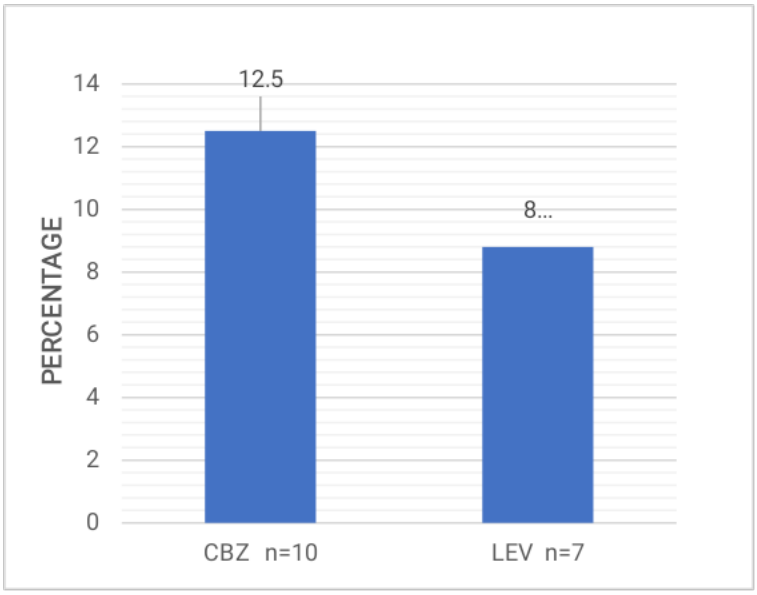

Figure 4.13: Comparison of the development of Seizures among 80 Participants each on LEV and CBZ Stroke cohort Treated at Three Selected Tertiary Hospitals from January 2019 to June 2021

LEV – Levetiracetam CBZ - Carbamazepine

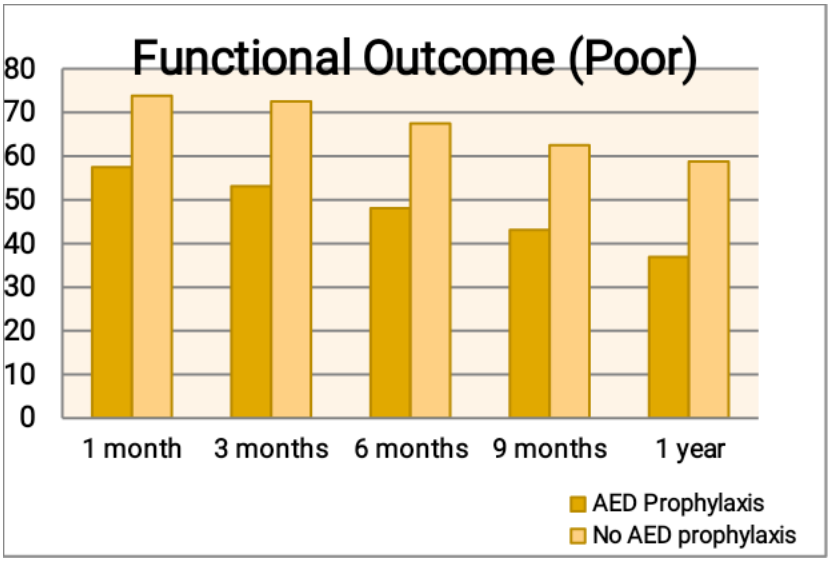

Figure 4.14: Comparison of outcome among 160 Stroke Patients on AED prophylaxis and 80 Stroke Patients not-AED prophylaxis Treated at Three Selected Tertiary Hospitals from January 2019 to June 2021

4.28: Comparison of EEG characteristics among 160 Stroke Patients on AED prophylaxis and 80 Stroke Patients not on AED prophylaxis Treated at Three Selected Tertiary Hospitals between January 2019 and June 2021

The section depicted by table shows EEG characteristics of two sessions at (160 AEDP vs 80 NAEDP) presentation and (119 AEDP vs 41 NAED) at 12months among 240 participants recruited in this phase of the study. With regards to presence of epileptiform pattern, 52(32.5%) of AED prophylaxis had epileptiform pattern which was lower compared to 48(60%) among no AED prophylaxis group and was statistically significant ($p \leq 0.001$). Furthermore, the percentage of participants in focal epileptiform, generalized and focal to secondary generalized epileptiform discharges were [9(5.6%) vs 6(7.5), [40(25%) vs 40(50%)], [3(1.9%) vs 2(2.5%)] and [108(67.5%) vs 32(40%)]. Concerning the background EEG changes at presentation, the frequency of alpha, theta, delta and intermixed were 70(43.8%), 56(35%), 31(19.4%) and 3(1.9%) respectively in the AED prophylaxis compare to 24(30%), 27(33.8%), 28(35%) and 1(1.3%) respectively in no AED prophylaxis group ($p \leq 0.046$). At 12months, the frequency of presence of epileptiform pattern, slowing and background EEG changes were comparable (See Table 4.29).

TABLE 4.29: EEG characteristics among 160stroke Patients on AED prophylaxis and 80 Stroke Patients not on AED prophylaxis Treated at Three Selected Tertiary Hospitals from January 2019 to June 2021

Variables	AEDP N(%)	NAEDP N(%)	x^2 value	p value
Background at presentation(n1=160.n2=80) Alpha Theta Delta Intermixed fast	70(43.8) 56(35) 31(19.4) 3(1.9)	24(30) 27(33.8) 28(35) 1(1.3)	8.020	0.046*
Background at 12months (n1=119,n2=41) Alpha Theta Delta Intermixed fast Intermixed slow	 88(73.9) 21(17.6) 9(7.6) 0(0) 1(0.8)	 32(78) 6(14.6) 2(4.9) 1(2.4) 0(0)	3.799	0.434
Epileptiform pattern at presentation (n1=160.n2=80) Focal Generalized Focal-generalized No	 9(5.6) 40(25) 3(1.9) 108(67.5)	 6(7.5) 40(50) 2(2.5) 32(40)	17.314	0.001*
Epileptiform pattern at 12months (n1=119,n2=41) Focal Generalized Focal-generalized No	 8(6.5) 24(19.5) 5(4.1) 86(69.9)	 3(7.3) 11(26.8) 1(2.4) 26(63.4)	1.214	0.750
Slowing at presentation (n1=160.n2=80) Focal Generalized Intermittent No	 1(0.6) 33(20.6) 45(28.1) 81(50.6)	 1(1.3) 32(40) 22(27.5) 25(31.3)	12.183	0.007*
Slowing at 12months (n1=119,n2=41) Focal Generalized Intermittent No	 0(0) 15(12.3) 30(24.6) 77(63.1)	 0(0) 6(14.6) 5(12.2) 30(73.2)	2.799	0.247

AEDP – Anti-Epileptic Drug Prophylaxis; NAEDP – No Anti – Epileptic Drug Prophylaxis; * $p<0.05$ comparing AEDP and NAEDP; n1 – Number of AEDP; n2

– Number of NAEDP

4.29: Comparison of the pattern of Mortality Rate among 160 Stroke Patients on AED prophylaxis and 80 Stroke Patients not on AED prophylaxis Treated at Three Selected Tertiary Hospitals from January 2019 to June 2021

Similarly, the MR was higher in the no AED prophylaxis group compare to the AED prophylaxis group. At 1month the MR 17(10.6%) in the AED prophylaxis group compared to 28(35.0%) in the no AED prophylactic group ($p<0.001$) at 1month. At 12months the MR 22(13.7%) in the AED prophylaxis group compared to 34(42.5%) in the no AED prophylactic group ($p<0.001$) (See Table 4.30).

Table 4.30: Pattern of Mortality Rate among 160 Stroke Patients on AED prophylaxis and 80 Stroke Patients not on AED prophylaxis Treated at Three Selected Tertiary Hospitals from January 2019 to June 2021

Variables	1month	3months	6months	12months
Medication				
n(%)	17(10.6)	19(11.9)	20(12.5)	22(13.7)
AEDP	28(35)	30(37.5)	33(41.2)	34(42.5)
NAEDP	<0.001*	<0.001*	<0.001*	<0.001*
p-value				
AED n(%)				
CBZ	8(10.0)	9(11.3)	9(11.3)	11(13.8)
LEV	9(11.3)	10(12.5)	11(13.8)	11(13.8)
p-value	0.798	0.807	0.633	1.000

*p<0.05 comparing either AEDP and NAEDP, or CBZ and LEV; CBZ – Carbamazepine; LEV – Levetiracetam; AED – Anti-Epileptic Drug; AEDP – Anti-Epileptic Drug Prophylaxis; NAEDP – No Anti – Epileptic Drug Prophylaxis

4.30: Assessment of Cognitive Function among 160 Stroke Patients with and 80 Stroke Patients without prophylactic use of Anti-Epileptic Drugs Treated at Three Selected Tertiary Hospitals from January 2019 to June 2021

Of the 240 patients recruited, 160 stroke patients were on AEDP, while 80 patients were in the NAEDP group. The overall CSID score at 1month was 51.02±24.81 in AEDP group which was higher compared to 33.0±30.23 in the NAEDP group (p≤0.001). The overall CSID score at 6months 50.97±25.98 was higher in AEDP group compared to 33.42±32.10.04 in NAED group (p≤0.001). The overall CSID score at 12months was 55.39±26.19 in AEDP group which was higher compared to 36.37±34.06 in NAEDP (p≤0.001).

Among the 160 participants in AEDP group, 80 participants was on CBZ while 80 was on LEV. The overall mean CSID score of participants in the CBZ group at 1month was lower 48.08±24.34 compared to participants in LEV group 53.96±25.08 and this was not statistically significant whereas at 12months, the overall mean CSID score of participants in the CBZ group was 53.71±26.41 which was lower compared to participants in the LEV group 57.01±25.90.

Furthermore, comparing the overall mean CSID score in those that developed seizures in the AEDP group at 12months, participants in CBZ group had a lower mean score of 25.90±35.10 compared to participants in LEV group with 61.29±16.28 and this was statistically significant (p≤0.015) (See Table 4.31, 4.32, 4.33).

Table 4.31: Assessment of Cognitive Function among 160 Stroke Patients and 80 Stroke Patients without prophylactic use of Anti-Epileptic Drug Treated at Three Selected Tertiary Hospitals from January 2019 to June 2021

Variables Mean(SD)	1month		p-value	6months		p-value	12months		p-value
	AEDP n=160	NAEDP n=80		AEDP n=160	NAEDP n=80		AEDP n=157	NAEDP n=78	
Language expression Language Naming Expression definition Expression Repetition Expression Fluency Total score Languagecompression Total language score	5.0(2.43) 3.60(1.75) 0.67(0.43) 3.41(1.80) 12.10(6.23) 3.61(1.61) 16.22(7.0)	3.30(2.94) 2.40(2.11) 0.41(0.50) 2.11(2.02) 8.21(7.42) 2.40(2.15) 10.61(9.52)	0.0001* 0.0001* 0.0001* 0.0001* 0.0001* 0.0001* 0.0001*	5.01(2.47) 3.60(1.77) 0.65(0.45) 3.38(1.77) 12.67(6.35) 3.60(1.79) 16.33(8.13)	3.21(3.09) 2.31(2.21) 0.41(0.48) 2.15(2.11) 8.15(7.78) 2.39(2.31) 10.28(10.05)	0.0001* 0.0001* 0.0001* 0.0001* 0.0001* 0.0001* 0.0001*	5.40(2.47) 3.86(1.75) 0.71(0.45) 3.95(2.00) 13.86(6.36) 3.79(1.81) 17.68(8.14)	3.47(3.22) 2.49(2.29) 0.46(0.49) 2.55(2.31) 8.91(8.28) 2.51(2.31) 11.38(10.57)	0.0001* 0.0001* 0.0001* 0.0001* 0.0001* 0.0001* 0.0001*
Memory Registration Delayed recall Short test Semantics Total score	2.70(1.42) 1.33(0.72) 3.0(2.20) 5.0(3.14) 13.87(7.49)	1.84(1.71) 0.94(0.90) 2.80(2.59) 4.11(3.70) 9.60(8.70)	0.0001* 0.0001* 0.0001* 0.0001* 0.0001*	2.66(1.50) 1.35(0.75) 3.89(2.28) 5.90(3.36) 13.68(7.88)	1.79(1.77) 0.90(0.89) 2.65(2.63) 3.96(3.85) 9.25(9.15)	0.0001* 0.0001* 0.0001* 0.0001* 0.0001*	2.85(1.53) 1.48(0.71) 4.22(2.35) 6.47(3.46) 15.08(7.96)	1.95(1.86) 0.99(0.92) 2.91(2.78) 4.42(4.18) 10.35(9.72)	0.0001* 0.0001* 0.0001* 0.0001* 0.0001*
Attention and calculation	5.08(2.91)	3.33(3.20)	0.0001*	5.33(2.92)	3.56(3.45)	0.0001*	5.97(2.96)	4.26(3.75)	0.0001

Orientation time Orientation place Orientation total score	2.90(1.41) 4.28(2.11) 7.14(3.51)	1.90(1.70) 2.90(2.52) 4.78(4.23)	0.0001* 0.0001* 0.0001*	2.89(1.45) 4.34(2.16) 7.23(3.61)	1.85(1.78) 2.80(2.66) 4.65(4.44)	0.0001* 0.0001* 0.0001*	3.11(1.44) 4.68(2.14) 7.82(3.58)	1.97(1.86) 3.0(2.79) 5.02(4.67)	* 0.0001* 0.0001* 0.0018*
Praxis Square Triangle with leg Chevron Rake Total score	 2.95(1.90) 2.04(1.11) 2.06(1.11) 2.10(1.10) 8.43(4.21)	 1.42(1.31) 1.41(1.30) 1.41(1.30) 1.50(1.30) 5.80(5.11)	 0.0001* 0.0001* 0.0001* 0.0001* 0.0001*	 2.08(1.10) 2.05(1.19) 2.07(1.10) 2.04(1.11) 8.25(4.39)	 1.39(1.34) 1.39(1.34) 1.38((1.34) 1.38(1.34) 5.54(5.35)	 0.0001* 0.0001* 0.0001* 0.0001* 0.0001*	 2.18(1.19) 2.14(1.14) 2.18(1.19) 2.14(1.14) 8.65(4.50)	 1.44(1.38) 1.44(1.38) 1.44(1.38) 1.44(1.38) 5.74(5.51)	 0.0001* 0.0001* 0.0001* 0.0001* 0.0001*
Overall total score	51.02(24.81)	33.0(30.23)	0.0001*	50.97(25.98)	33.42(32.10)	0.0001*	55.39(26.19)	36.37(34.06)	0.0001*

*p<0.05 COMPARING AEDP and NAEDP; AEDP – Anti – Epileptic Drug Prophylaxis; NAEDP – No Anti – Epileptic Drug Prophylaxis; SD – Standard Deviation

Table 4.32: Assessment of Cognitive Function between 80 stroke patients on CBZ and 80 stroke patients on LEV prophylaxis treated at three selected tertiary hospitals from January 2019 to June 2021

Variables Mean±SD)	1month		p-value	6months		p-value	12months		p-value
	CBZ n=80	LEV n=80		CBZ n=80	LEV n=80		CBZ n=77	LEV n=80	
Language expression									
Language Naming	4.59(2.37)	5.40(2.43)	0.035*	4.66(2.40)	5.36(2.50)	0.071	5.17(2.45)	5.63(2.48)	0.241
Expression definition	3.28(1.69)	3.86(1.77)	0.035*	3.33(1.71)	3.86(1.80)	0.058	3.70(1.72)	4.01(1.72)	0.275
Expression Repetition	0.62(0.43)	0.73(0.43)	0.122	0.58(0.46)	0.71(0.44)	0.067	0.65(0.47)	0.77(0.42)	0.094
Expression Fluency	3.04(1.68)	3.78(1.79)	0.009*	3.11(1.71)	3.66(1.80)	0.046*	3.69(1.80)	4.21(2.16)	0.106
Total score	11.54(5.97)	13.76(6.31)	0.023*	1.68(6.12)	13.66(6.46)	0.047*	13.21(6.34)	14.49(6.35)	0.208
Language compression	3.27(1.78)	3.85(1.78)	0.038*	3.34(1.74)	3.86(1.80)	0.066	3.61(1.83)	3.98(1.79)	0.201
Total language score	14.83(7.70)	17.61(8.09)	0.027*	15.10(7.85)	17.55(8.28)	0.057	16.84(8.14)	18.48(8.12)	0.211
Memory									
Registration	2.56(1.38)	2.76(1.47)	0.376	2.56(1.47)	2.76(1.54)	0.402	2.84(1.50)	2.85(1.57)	0.981
Delayed recall	1.30(0.68)	1.36(0.77)	0.587	1.29(0.75)	1.41(0.74)	0.290	1.47(0.70)	1.50(0.73)	0.776
Short test	3.88(2.14)	4.10(2.25)	0.518	3.78(2.23)	4.00(2.34)	0.535	4.25(2.27)	4.20(2.43)	0.901
Semantics	5.69(3.09)	6.21(3.18)	0.297	5.73(3.29)	6.08(3.44)	0.519	6.47(3.37)	6.47(3.37)	0.980
Total score	13.31(7.24)	14.35(7.51)	0.372	13.21(7.71)	14.16(8.06)	0.444	15.10(8.22)	15.05(8.22)	0.966

Attention and calculation Orientation time Orientation place Orientation total score	4.87(2.78) 2.65(1.36) 3.93(2.07) 6.58(3.42)	5.30(3.02) 3.06(1.44) 4.64(2.11) 7.70(3.54)	0.348 0.064 0.032 * 0.042 *	5.11(2.78) 2.71(1.42) 4.09(2.12) 6.80(3.54)	5.54(3.06) 3.06(1.46) 4.59(2.19) 7.65(3.65)	0.360 0.127 0.144 0.137	5.97(2.89) 2.94(1.45) 4.45(2.14) 7.44(3.58)	5.97(3.04) 3.27(1.42) 4.90(2.14) 8.18(3.56)	0.998 0.141 0.194 0.200
Praxis Square Triangle with leg Chevron Rake Total score	1.88(1.06) 1.88(1.06) 1.90(1.05) 1.98(1.04) 7.90(4.16)	2.23(1.09) 2.20(1.10) 2.23(1.09) 2.21(1.10) 8.94(4.32)	0.044 * 0.064 0.056 0.162 0.124	1.96(1.08) 1.96(1.08) 1.93(1.09) 1.93(1.09) 7.80(4.33)	2.20(1.10) 2.15(1.13) 2.20(1/.10) 2.15(1.13) 8.70(4.44)	0.160 0.270 0.123 0.216 0.197	2.12(1.12) 2.09(1.13) 2.12(1.12) 2.09(1.12) 8.42(4.49)	2.24(1.12) 2.20(1.15) 2.24(1.12 2.20(1.15) 8.88(4.51)	0.479 0.565 0.479 0.574 0.523
Overall total score	48.08(24.34)	53.96(25.08)	0.134	48.03(25.78)	53.91(26.01)	0.152	53.71(26.41)	57.01(25.90)	0.431

*p<0.05 comparing CBZ and LEV SD – Standard Deviation CBZ – Carbamazepine LEV – Levetiracetam

Table 4.33: Trend of Cognitive Function between 10 Stroke Patients on Carbamazepine and 7 Stroke Patients on Levetiracetam prophylaxis that developed Stroke Induced Epilepsy Treated at Three Selected Tertiary Hospitals from January 2019 to June 2021

Variables Mean±SD)	12months		p-value
	CBZ n=10	LEV n=7	
Language expression			
Language Naming	2.45±3.32	5.93±1.43	0.021*
Expression definition	1.75±2.37	4.07±1.17	0.031*
Expression Repetition	0.35±0.47	0.93±0.19	0.008*
Expression Fluency	1.75±2.37	4.07±1.17	0.031*
Total score	6.30±8.54	15.00±3.87	0.024*
Language	1.75±2.37	4.07±1.17	0.031*
compression	8.10±10.93	19.14±4.92	0.025*
Total language score			
Memory			
Registration	1.40±1.90	3.43±0.79	0.018*
Delayed recall	1.57±0.53	1.57±0.53	0.045*
Short test	2.10±2.85	5.00±1.29	0.024*
Semantics	3.15±4.27	7.50±1.94	0.024*
Total score	7.50±10.02	17.71±4.15	0.023*
Attention and	2.80±3.79	6.29±2.14	0.013*
calculation	1.40±1.90	3.43±0.79	0.018*
Orientation time	2.10±2.85	5.00±1.29	0.024*
Orientation place	3.50±4.74	8.43±2.07	0.022*
Orientation total score			
Praxis			
Square	1.05±1.42	2.50±0.65	0.024*
Triangle with leg	1.05±1.42	2.50±0.65	0.024*
Chevron	1.05±1.42	2.50±0.65	0.024*
Rake	1.05±1.42	2.50±0.65	0.024*
Total score	4.20±5.69	10.00±2.58	0.024*
Overall total score	25.90±35.10	61.29±16.28	0.015*

*p<0.05 comparing LEV and CBZ; CBZ – Carbamazepine; LEV – Levetiracetam;

SD – Standard Deviation

4.31: Comparison of Mean Time to Seizure onset, Seizure duration and time to Seizure stoppage among 160 Patients on Anti-Epileptic Drug Prophylaxis and 80 Patients on Non Anti-Epileptic Drug Prophylaxis Treated at Three Selected Tertiary Hospitals from January 2019 to June 2021

Among 240 patients recruited, 160(67%) were in the AEDP group and 80(33%) were in the NAEDP group. Among the 160(67%) in the AEDP group, the mean seizure duration in days in CBZ group was 55.70±69.84 compared to the value of 96±65.15 in LEV group which was not significant (p≤0.248). Among the CBZ group, the mean time to seizure onset in days was 58.0±83.57 which was shorter compared to the mean value of 183.43±156.19 in the LEV group and this was statistically significant (p≤0.041). Furthermore, the mean time to seizure stoppage in days was 108.60±145.53 in the CBZ group which was shorter compared to the mean value of 271.43±75.54 in the LEV group and this was statistically significant (p≤0.016) (See Table 4.34).

Table 4.34: Comparison of Mean Time to Seizure onset, Seizure duration and time to Seizure stoppage among 160 Patients on Anti-Epileptic Drug Prophylaxis and 80 Patients on Non Anti-Epileptic Drug Prophylaxis Treated at Three Selected Tertiary Hospitals from January 2019 to June 2021

Variables	CBZ (Mean±SD)	LEV (Mean±SD)	None (Mean±SD)	F Value	p1Value	T – test	p2 Value
Duration in Days	55.70±69.84	96±65.15	89.59±122.02	0.465	0.632	-1.202	0.248
Time Seizure Started	58.90±83.57	183.43±156.19	58.29±81.00	4.541	0.019*	-2.239	0.041*
Time Seizure Stopped	108.60±145.53	271.43±75.54	141.88±158.02	2.951	0.067	-2.699	0.016*

*p<0.05; LEV-Levetiracetam; CBZ-Carbamazepine;

F value- statistics comparing CBZ, LEV and None;

p1 value- comparing CBZ, LEV and None; T test- statistics comparing CBZ and LEV;

p2 value- comparing CBZ and LEV only; SD – Standard Deviation

4.32: Comparison of EEG characteristics among 80 Patients each on Carbamazepine and Levetiracetam prophylaxis Treated at Three Selected Tertiary Hospitals from January 2019 to June 2021

This section as shown on Table 4.35 describes EEG characteristics at presentation and 12month in patient on LEV and CBZ prophylaxis. With regards to EEG background at presentation, there was lower alpha background [28(35%) vs 42(52.5%)], higher theta background [29(36.3%) vs 27(33.8%)], higher delta background [21(26.3) vs 10(12.5%], and higher intermixed fast background [2(2.5%) vs 1(1.3%)] in participants on CBZ compared to LEV prophylaxis and this was statistically significant (p≤0.023).

At presentation, there were lower focal epileptiform [6(7.5%) vs 3(3.8%)], higher generalized epileptiform [25(31.3%) vs 15(18.8%)], lower focal-generalized epileptiform [1(1.3%) vs 2(2.5%)] and lower no epileptiform pattern [48(60%) vs 60(75%)] in participants on CBZ compared to those on LEV and this was statistically significant (p≤0.001).

At 12month, there were higher focal epileptiform [6(10.3%) vs 2(3.1%)], higher generalized epileptiform [15(25.9%) vs 9(13.8%)], lower focal-generalized epileptiform [1(1.7%) vs 4(6.2%)] and lower no epileptiform pattern [36(62.1%) vs 50(76.9%)] in participants on CBZ compared to those on LEV but this was not statistically significant (p≤0.215).

Table 4.35: Comparison of EEG characteristics among 80 Patients each on Carbamazepine and Levetiracetam prophylaxis Treated at Three Selected Tertiary Hospitals from January 2019 to June 2021

Variables n(%)	CBZ	LEV	None	p value
Background at presentation (c=80, l=80,n=80)				
Alpha	28(35)	42(52.5)	24(30)	0.023*
Theta	29(36.3)	27(33.8)	27(33.8)	
Delta	21(26.3)	10(12.5)	28(35)	
Intermixed fast	2(2.5)	1(1.3)	1(1.3)	
Background at 12months (c=57, l=62, n=41)				
Alpha	38(66.7)	50(80.6)	32(78)	0.283
Theta	11(19.3)	10(16.1)	6(14.6)	
Delta	7(12.3)	2(3.2)	2(4.9)	
Intermixed slow	1(1.8)	0(0)	1(2.4)	
Epileptiform pattern at presentation (c=80, l=80, n=80)				
Focal	6(7.5)	3(3.8)	6(7.5)	0.001*
Generalized	25(31.3)	15(18.8)	40(50)	
Focal-generalized	1(1.3)	2(2.5)	2(2.5)	
No	48(60)	60(75)	32(40)	
Epileptiform pattern at 12months (c=57, l=62, n=41)				
Focal	6(10.3)	2(3.1)	3(7.3)	0.215
Generalized	15(25.9)	9(13.8)	11(26.8)	
Focal-generalized	1(1.7)	4(6.2)	1(2.4)	
No	36(62.1)	50(76.9)	26(63.4)	
Slowing at presentation (c=80, l=80, n=80)				
Focal	0(0)	1(1.3)	1(1.3)	0.001*
Generalized	25(31.3)	8(10)	32(40)	
Intermittent	21(26.3)	24(30)	22(27.5)	
No	34(42.5)	47(58.8)	25(31.3)	
Slowing at 12months (c=57, l=62, n=41)				
Focal	0(0)	0(0)	0(0)	0.003*
Generalized	13(22.8)	2(3.1)	6(14.6)	
Intermittent	9(15.8)	21(32.3)	5(12.2)	
No	35(61.4)	42(64.6)	30(73.2)	

*p<0.05 comparing CBZ and LEV LEV: Levetiracetam CBZ: Carbamazepine p value - comparing CBZ and LEV only

CHAPTER FIVE

DISCUSSION

5.1: Hospital-based pattern of Epilepsy among adult (and adolescent) Nigerians in South Western Nigeria

In the first phase of the study which is among cohort of epilepsy patients, there is preponderance of female sex (sex ratio 0.89), a finding which is similar to previous reports from some studies in Nigeria, Rwanda, Tanzania (Assadeck *et al.,* 2019*;* Hirose, 2014; Nwani *et al.,* 2013; Osuntokun *et al.,* 1987). Findings of the majority of the participants aged 18 and 35 years is in tandern with demographics. It is noteworthy that 79% of Nigerians are below the age of 35/40 years (NPC, 2006). Further, CNS infections especially parasitic infections like neurocysticercosis, trauma, birth asphyxia and other perinatal morbidity, ineffective immunization strategy against communicable diseases, poverty and lower standard of living are possible additional reasons for higher figures of epilepsy among adolescents and young adults *(*Paul *et al.,* 2012; Singh *et al.,* 2022*).* Previous meta-analysis showed bimodal age group among patients with epilepsy which is similar to finding from this current study that showed there were more epilepsy patients in the 18-35 years and 36-60 years age group*(*Paul *et al.,* 2012).

In majority of cases, there was no obvious cause, however, epilepsy was observed to be commonly due to stroke. Similar findings have been documented previously (Ogunrin *et al*., 2013; Wagner *et al.,* 2015). The consistent unfavorable changes in EEG findings in the background, slowing and epileptiform pattern in the SIS compared to NSIS underscores the additive risk and burden that structural epilepsy like SIE/SIS poses on epilepsy management and outcome.

Nearly a third of the studied patients did not receive AED prescription, immediate explanation could not be adducted to the serious Treatment Gap (TG) which may be worsened by other determinants of nonadherence to medication. TG documented in previous studies ranges from 23% to as high as 90% *(*Assadeck *et al.,* 2019; Guinhouya *et al.,* 2010; Singh *et al.,* 2022 Owolabi *et al.,* 2020*)*.

Five hundred and fifteen, 515 (79.0%) of those on AEDs) received CBZ, 85 (13.0%) received LEV. The finding is in consonance with the reports from other studies that reported over 70% to 97.5% use of CBZ among cohort of people living with epilepsy in SSA *(*Assadeck *et al.,* 2019*;* Nwani *et al.,* 2013; Owolabi *et al.,* 2020; Sanya *et al.,* 2013*)*. Comparatively, prescription of LEV, a new generation AED, in this study was high given findings from similar studies in sub-Saharan African. For example, studies by Assadeck and colleagues had limited access to newer AEDs and only 45(72.6%) CBZ 15(24.2%) PHB and PHB 15(3.2%) among the epileptic patients (Assadeck *et al*., 2019). It was also observed that epilepsy was mostly managed using monotherapy though nearly a third of the respective patients required more than one medication. Adverse drug effect, drug interactions, cost, poor adherence acting individually or collectively recommend against the use of more than one AED.

5.2: Pattern and clinical predictors of Seizure disorders among stroke survivors

In the second phase, twenty-seven percent of individuals who suffered stroke developed seizure. The affected patients had worse overall mortality, more severe stroke when compared to the Non-Stroke Induced Seizure (NSIS) cohort. These finding are consistent with other previous finding with regards to effect of SIS on stroke outcome (Lahti *et al*., 2017; Xu, 2019).

The risk of developing SIS was revealed to be about 12% stroke survivor in the OCSP within five years, while *Naess and colleagues* reported that 10.5 developed SIE at 5.7 years in population based study.(Burn *et al*., 1997) In a study to determine the prevalence and predictors of SIE among Ghanaians

stroke survivors between 2018 and 2020 among 1101 stroke patients 126(11.4) developed SIE at a mean age of 57.7 identified predictors of SIE were male, cortical ischemic stroke, higher blood pressure and number of anti-hypertensive drugs *(*Sarfo *et al.,* 2020*).* The prevalence of 11.4 in the Ghanaian study is about half of the 27% found in this current study among Nigeria cohort. The difference in the two studies might be due to study design, sample size, patient choice, and extent neurophysiological evaluation. The Ghanaian study was cross – sectional among ambulatory stroke cohort with presumably less severe stroke and EEG was not done, while the current study is prospective among stroke patient regardless of the severity or ambulatory status and neurophysiological evaluation using EEG was carried out. In another study, profiling characteristics of SIE in the main reference centre among Burkina Faso stroke cohort, 32 out of 116 patients has SIE with mean age of 58. Again, male gender was identified as a significant risk factor *(*Napon *et al.,* 2016*).* In this current study, there was no association between male gender and SIE but there was an association between gender and mortality. A previous study in Benin, Nigeria had recorded about 10% occurrence of SIS whereas findings in this study indicate more than a quarter of stroke survivors developed seizure. It is noteworthy that the former was a retrospective study which did not include EEG evaluation, therefore, the apparent discordance may be a reflection of the different design, at least, in part (Aiwansoba and Chukwuyem, 2014). Nevertheless, it is becoming more evident that SIS and SIE are under diagnosed and underestimated without proper clinical and neurophysiological evaluation (Bentes *et al.*, 2018). More recently, in a large multicenter study aimed at determining frequency and factors associated with SIS among Nigeria cohort, of the 12 potential factors linked with SIS namely Age, income, hypertension, dyslipidemia, cardiac disease, family history of stroke, recurrent use of salt, fish consumption, stroke type, white blood cell count, volume of lesion and length of stay on admission, only age, stroke severity as measured by NHISS and white blood cell count were independently associated with SIS (Sarfo *et al.*, 2021).

This current study however identified presence of diabetes mellitus and NIHSS

at presentation as the predictors of SIS while cortical involvement on brain imaging, sleep disorder and presence of epileptiform pattern at presentation as the predictors of SIE among variable. A consistent finding among previous studies which was further alluded by this current study is that cortical involvement on brain imaging and stroke severity are major determinant of SIS/SIE (Huang *et al.*, 2014; Tanaka *et al.*, 2015). The finding of lower CSID scores indicating poorer cognitive function among SIS group compared to those without SIS is unexpected because of additional risk of cognitive dysfunction from SIS/SIE. Previous studies identified depression, seizure severity, type, pharmaco-resistance, duration of epilepsy, age of onset, severity of epileptic activity, ictal and interictal epileptiform pattern, and underlying acquired and structural lesion are identified risk factor of cognitive impairment (Loughman *et al.,* 2017; Taylor *et al.,* 2011; Chan*, et al.,* 2018). Cognitive impairment has been described as one of the complications of stroke. Silent infarcts and microhemorrhages inflict subtle cumulative brain damage resulting in cognitive decline due to direct consequence of vascular lesions or pre-existing neuropathology like disruption of BBB with chronic leakage of fluid and macromolecules in the white matter, inflammatory and genetic factors (Akinyemi *et al.,* 2019; Goulay *et al.,* 2019; Liu *et al.,* 2018). The distinguishing features for vascular cognitive impairment are frontal and subcortical dysfunction typically manifesting as slowness, executive dysfunction, behavioural and mood changes, and speech deficit *(*Akinyemi *et al.,* 2021; Owolabi *et al.,* 2018*).*

Identified mechanisms of cognitive dysfunction are programmed cell death, release of excitatory and reduction of inhibitory neurotransmitter, neuronal loss, nutrient deprivation, depletion of choline acetyltransferase CAT and deficiency of survival factors BCL2,p53 and neurotoxins (Farooq and Gorelick, 2013; Horvath *et al.,* 2020; Rayner *et al.*, 2016; Sen *et al.*, 2018). Overall, aside additional cognitive risk, SIS after stroke has worse severity, poor outcome, and high mortality rate.

The consistent finding of EEG Epileptiform pattern which was more common

in SIS/SIE group compared to NSIS group from presentation to 12months is in consonance with previous findings which identified epileptiform pattern on EEG as risk factor for SIE and maker of poor prognosis (Bentes *et al.,* 2018; Mecarelli *et al.*, 2011). EEG monitoring in acute stroke is key but underutilized area that can aid recognition of electrographic/subclinical seizures, the detection of regional ischemia, and prognostication. Early presence of interictal epileptiform pattern, periodic discharges, asymmetry predicts SIE, prolonged hospital stay, and mortality in acute stroke (Bentes *et al.*, 2018). The yield of EEG activity increases with continuous and repetitive monitoring, however, there are still limitations to predictive and prognostic value of EEG in stroke management (Doria and Forgacs, 2019).

Overall, the clinical, radiological, and neurophysiological findings should be factored into prediction model that can predict SIE and its mortality in our environment.

5.3: Comparative Efficacy and Tolerability of Levetiracetam and Carbamazepine in Stroke` Induced Epilepsy

In the third phase of the study, we found higher MR, higher NIHSS score indicating poorer outcome, higher participants with unfavourable outcome, were more in the CBZ compared to LEV group.

Treatment have been empirical, with older AEDs like CBZ, PHT and sodium valproate but this is without issues on side effect, drug-drug interactions and tolerability which are less compare to with newer AEDs like LEV (Abou-Khalil, 2016; Ouerdiene *et al.*, 2021). Data from previous studies on clinical efficacy of AED in SIE supports use of second-generation AED like LEV and gabapentin as viable treatment of lower reoccurrence rate and fewer side effects. The role of AED in the treatment of SIS, perhaps, too, in its prevention, is becoming more apparent, however, the choice of drug and time of introduction may require more data. Many factors will direct the choice of AEDs in treatment of SIS from tolerability, age of patient, drug-drug interactions, and cost. Inhibition of microglial activation, activation and down regulation of inflammatory mediator

release and alteration of neurotransmitter level are some of mechanism of AEDs in SIS.

The use and choice of newer AEDs is on increase due to less side effects and fewer drug interactions. LEV has been suggested as an alternative for older AEDs against SIS, based on safety and efficacy profiles in clinical studies.

Overall, this study revealed LEV performed better than CBZ in treatment of SIS with regards to occurrence of seizure, preservation of cognitive function. Studies have previously established that LEV has safety profile, and fewer drug interactions when compared to CBZ (Alzueta *et al.,* 2018*;* Wood and Gillard, 2017*).* Few studies have also suggested that LEV possesses neuroprotective effect which might have been responsible for the better outcomes observed in this study *(*Berlin *et al.,* 2019*;* Harby *et al.,* 2020; Sourbron *et al.,* 2018). However, available data supports a trend for controlled release CBZ to be associated with fewer AEs when compared to immediate release CBZ; hence, if CBZ is to be used, controlled release formulation is preferable *(*Baulac *et al.,* 2014*;* Brigo *et al.,* 2018*).*

Furthermore, in this study, cohort on LEV had better CSID scores across all domain of cognition which indicate better cognitive status compared to those on CBZ. Previous documentation has described superiority of LEV over CBZ in patients with epilepsy (Alzueta *et al*., 2018; Brigo *et al*., 2018). Another previous study, associated LEV with improved cognitive or neural functional outcomes after Intracerebral haemorrhage (Taylor *et al.,* 2011).

Conclusively in the third phase of this study, the burden of SIS is substantial and significantly contribute to morbidity and mortality, LEV performed better with regards to MR, functional outcome, cognitive status, occurrence of epileptiform pattern on EEG compared to CBZ in treatment of SIE.

5.4: Evaluation of the role of Levetiracetam and Carbamazepine in the prevention of Stroke Induced Seizure/Stroke Induced Epilepsy

In the fourth phase of the study, the use of AEDs, LEV or CBZ, reduced occurrence of SIS, and LEV demonstrated better profile than CBZ. These findings will be expected to assist in the adequate management of stroke survivors, improve outcomes, and contribute to their quality of life, if same can be replicated in larger studies. It is noteworthy that there are controversies with regards to AEDs prophylaxis as some guidelines recommend against the use of AED for prophylaxis due to lack of reliable RCT (Ouerdiene *et al.*, 2021; Xu, 2018).

This study revealed higher MR, poorer outcome on MRS and CSID score in NPG compared with PG. However, comparing the two AEDs, apart from the fact that it took a longer time for seizure to develop in the LEV group compared to the CBZ group, there was higher seizure occurrence in the CBZ group. These finding further supports recent finding of antiepileptogenic role of LEV in clinical and animal studies (Smedt *et al.*, 2007; Lyseng-Williamson, 2011).

Identifying agent with antiepileptogenic properties which will prevent and/or reduce seizure occurrence remains an important end point in management of epilepsy (Vinogradova and van Rijn, 2008). Surprisingly, the mean time of seizure stoppage was longer in the LEV group compared to CBZ group and NPG, this can be explained by higher MR leading shorter duration in the CBZ group. It thus appears that while LEV and CBZ are useful for secondary prevention of SIE, only LEV exhibited better prophylactic activity. Overall, fourth study revealed that the use of AED reduces mortality and associated with better cognitive and functional outcome with LEV exhibiting better therapeutic effect than CBZ for prophylaxis.

CHAPTER SIX

SUMMARY, CONCLUSION AND RECOMMENDATIONS

6.1: Summary

Newer AEDs like Levetiracetam (LEV) have better safety and tolerability profiles, however there is limited clinical evidence supporting its use in the treatment and prevention of PSE. This multi-centred and multi-stage study identified determinants of PSE and compared prophylactic and therapeutic effects of LEV and CBZ monotherapy.

The aetiology of majority of epilepsy remains to be elucidated, however, stroke is the commonest cause among the adolescent and adult Nigerian population studied after idiopathic group. Females were slightly more than males, and there was no evidence of use of AEDs in nearly a third of all patients studied. CBZ was the most frequently prescribed anti-epileptic drug. Diabetes mellitus and NIHSS at presentation were predictive of SIS while cortical involvement on brain imaging, sleep disorder and presence of epileptiform pattern at presentation appeared to be predictors of SIE.

Poststroke seizure was diagnosed in more than a quarter of participants in (the prospective phase of) the study, which negatively affect outcome. Levetiracetam demonstrated superior therapeutic effects compared to Carbamazepine. In comparison with negative control, both LEV and CBZ impacted positively on survivor, cognition, when used as prophylactic agents among stroke patients.

6.2: Conclusion

Stroke severity, cortical involvement, epileptiform pattern and background diabetes mellitus were identified as predictors of post stroke epilepsy. Levetiracetam exhibited better therapeutic effect than carbamazepine for prophylaxis and treatment of post stroke epilepsy

6.3: Recommendations

Prophylactic use of AED is essential in at risk individuals based on volume, size, severity, ventricular involvement, and EEG findings that predispose to development of SIE.

Undoubtedly, more research works are needed to guide choice, dosage, possible time of intervention, and length of therapy after exposure to the initial insults cascading process of epileptogenesis.

6.4: Contributions to Knowledge

This study is one the few studies that evaluated prophylactic role and efficacy of AEDs in SIS/SIE. Furthermore, the EEG evaluation removed the bias of under estimation of SIS/SIE as previously documented. To the best of my knowledge, this will be the first study comparing efficacy and prophylactic role of LEV and CBZ in SIS/SIE in our environment. The beneficial effect and risk of preventive use of AEDs in stroke survivors have not been studied in clinical trials especially in our environment.

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APPENDIX I

INFORMED CONSENT

Institutional Ethical approval number: _____

I am Dr. Luqman Opeoluwa Ogunjimi, a staff of department of Pharmacology and Therapeutics, at Olabisi Onabanjo University and a postgraduate student at University of Ibadan in the Department of Pharmacology and Therapeutics. The aim of this study is to evaluate beneficial of antiepileptic drug on post stroke seizure and epilepsy.

In the course of this research, I will be asking you some important questions about stroke, epilepsy and your medications and later carry out physical examinations on you. This examination will not inflict any pain on you. Also, a small electrode will be placed on your head to measure some brain activity. Furthermore, the process will involve taking blood sample for analysis. The procedure of taking blood sample will cause slight pain when the syringe is introduced into your vein. kindly note that you are not paying any money at any stage of this study and withdrawal at wish is possible without any form of bias in treatment after withdrawing. I will be requiring your kind permission to make use of brain imaging during course of research. Be rest assured that information obtained from you will be kept confidential.

(This was explained in details and translated to local languages that participant understood, where the participant is not capable giving consent, the relative/care giver in charge gave will be involved)

Statement of individual collecting informed and understood consent:

I explained in details this research to _____and adequate information given with risks and benefits

Name:.....

Signature/thumbprint……

Date of obtaining consent.....

Statement from consenting participant:

I have good understanding of the research after it was described in detail and translated to local language that am comfortable with and easy for me to

understand. It is clear to me that my involvement in the process is voluntary and I can decide to withdraw at any point in time. The reason, benefits, possible risk and procedure involved in the research are abundantly clear to me.

I have collected a copy of this consent form and additional information sheet to keep for myself.

Name: .....

Signature of participant giving consent……..

Date.....

Signature of witness: .....

Name of witness: .....

The approval for this research was given by the Institution Review Board on Research and ethics of the selected centers.

Furthermore, if you need any clarification about the study at any stage, you can contact Dr Luqman Opeoluwa Ogunjimi, Department of Pharmacology and Therapeutics Olabisi Onabanjo University. Mobile:07032683222. E-mail: luqmanogunjimi@yahoo.com

APPENDIX II

QUESTIONAIRE

DATE: _____ ID NO_____

(A) Demographic Data

Surname: _____ Other Names _____

Address:_____

_____

State_____ City_____

Gender: Male Female Date of Birth: Age

Handedness:_____ Telephone No: _____

Marital Status Formal Education Occupation: _____

Average Total Monthly Household Income (in USD) Living Situation

- ☐ 0-100
- ☐ 100-250
- ☐ 1250-500
- ☐ 1501-1500
- 1501-3000

- ☐ Lives alone
- ☐ Lives with Spouse alone
- ☐ Lives with Spouse and Children
- ☐ Lives in a nursing Home
- ☐ Lives with Extended Family

Ethnic Group: **Languages Spoken:**

Yoruba: ☐ Igbo: ☐ Hausa: ☐ Others: _____ English ☐ Yoruba ☐ Hausa ☐ Igbo Others: _____

Contact: Spouse, Next of Kin or Friend.

Surname:_____ Other Names: _____ Telephone:_____

(B) Laboratory Results

1. FBC

Packed Cell Volume% ……

White Cell Count(mm)…….

Platelets(x10/min)…….

White Blood Cell differentials (%)

Neutrophils ☐ Lymphocyte ☐ Mo ☐ ☐ Eosinophils

Basophil ☐

2. RED CELL INDICES	**3. ELECTROLYTE**	**4. GLYCEMIC INDEX**
RBC _____	Sodium: _____	Random Glucose_____
HGB _____	Potassium:_____	Fasting Glucose:_____
HCT: _____	Urea _____	HBAIc_____
MCV _____	Creatinine: _____	2HPP: _____

MCH: _____ Bicarbonate_____

MCHC:_____ Chloride: _____

RDW_____

5. PLATELET INDICES

PLT _____

MPV: _____

PCT: _____

PDW: _____

6. LIPID PROFILE

Triglyceride: _____

Total Cholesterol: _____

LDL-Cholesterol: _____

HDL-Cholesterol: _____

LDL/HDL Ratio: _____

STROKE VERIFICATION

1. CT: ☐ Ye☐ No ☐ **MRI:** ☐ Yes ☐ No

3. Angiography: ☐ Yes ☐ No

4. TIMINIG OF FIRST SCAN AFTER ONSET SYMPTOMS (HRS/DAYS/WEEKS)

☐ 0-24hrs ☐ 24-48hrs ☐ 48-72hrs ☐ 72hn-1wk ☐ 1wk-2wks

5. STROKE SUBTYPE (WITH RESULT OF BRAIN CT/MRI SCAN)

☐ **Iscemic** ☐ Haemorr☐ Both

6. STROKE LOCATION:

ACA ☐ MCA PCA ☐ WATER SED ☐

7. SMASH U:

i). Structural; Yes ☐ No ☐ Not applicable ☐

ii).Medication Related: Yes ☐ No ☐ Not applicable ☐

iii) Angiopathy: Yes ☐ No ☐ Not applicable ☐

iv) Systemic Disease: Yes ☐ No ☐ Not applicable ☐

v) Hypertension: Yes ☐ No ☐ Not applicable ☐

vi) Undetermined Yes ☐ No ☐ Not applicable ☐

8. INTRACEREBRAL HAEMORRHAGE SCORE (ICH SCORE):

1. Intracerebral Glasgow Coma Scale: 1. (13-15) 2.(5-12) 3.(3-4)

2. Intracerebral Haemorrhage Volume: 1->30 0=30

3. Intraventricular Haemorrhage: 0=No 1=Yes

4. Intracerebral Haemorrhage Age: 0=<80 1= >80.

5. Infratentorial origin: Yes ☐ No ☐

6. Total Score: _____

7. Volume: _____

OCSP CLASSIFICATION

a) TACI b) PACI c) POCI d) LACI e) Not applicable

10. TOAST

Small vessel:	Yes ☐	No ☐	Not applicable ☐
Large vessel:	Yes ☐	No ☐	Not applicable ☐
Cardioembolism:	Yes ☐	No ☐	Not applicable ☐
Undetermined	Yes ☐	No ☐	Not applicable ☐
Determined	Yes ☐	No ☐	Not applicable ☐

11. HYPERACUTE ISCHAMIC CHANGES:

1. Hyperdense Middle Artery	Yes ☐	No ☐	Not applicable ☐
2. Dot Sign	Yes ☐	No ☐	Not applicable ☐
3. Loss of Gray White Matter Differentiation	Yes ☐	No ☐	Not applicable ☐
4. Loss of Insular Ribon:	Yes ☐	No ☐	Not applicable ☐
5. Loss of Basal Ganglia Outline or Obstruction of Lentiform Nucleus:	Yes ☐	No ☐	Not applicable ☐

12. OTHER FINDINGS

6. Mass Effect:	Yes ☐	No ☐	Not applicable ☐
7.Ventricular Effacement:	Yes ☐	No ☐	Not applicable ☐
8. Sulca Effacement	Yes ☐	No ☐	Not applicable ☐
9. Mid-line Shift	Yes ☐	No ☐	Not applicable ☐
10. Uncal Herniation:	Yes ☐	No ☐	Not applicable ☐
13. Cerebral Atrophy:	Yes ☐	No ☐	Not applicable ☐

i) Peripheral:	Yes ☐	No ☐	Not applicabl ☐
ii) Central:	Yes ☐	No ☐	Not applicabl ☐
in) Periventricular:	Yes ☐	No ☐	Not applicabl ☐
iv) Tumor:	Yes ☐	No ☐	Not applicabl ☐

20. CT

1. Stroke Location A) Cortical B) Cortical-Subcortical C) Subcortical

2. Stroke Type A) Ischemic B) Hemorrhagic

3. Stroke Circulation

i) Anterior Cerebral Artery	Yes ☐	No ☐
ii) Middle Cerebral Artery	Yes ☐	No ☐
iii) Posterior Cerebral Artery	Yes ☐	No ☐
4. Subarachnoid Haemorrhage	Yes ☐	No ☐
i) Perimesenchphalic	Yes ☐	No ☐
ii) Basal	Yes ☐	No ☐
ii) Cistern	Yes ☐	No ☐
iv) Sylvian	Yes ☐	No ☐
5. Stroke Hemisphere	(A) Right (B) Left (C) Bilateral	
6. Age of Infarct	(A) Acute (B) Subacute (C) Cronic	
7.Size of Stroke:_____	Yes ☐	No ☐
8.StrokeVolume:_____	Yes ☐	No ☐
9. Intraventricular Extension	Yes ☐	No ☐
10. Basal Ganglia	Yes ☐	No ☐
a) Caudate	Yes ☐	No ☐
b) Lentiform	Yes ☐	No ☐
Lobar Involvement:	Yes ☐	No ☐
11. Frontal Lobe	Yes ☐	No ☐
12. Parietal Lobe	Yes ☐	No ☐

13. Temporal Lobe	Yes ☐	No ☐
14. Occipital Lobe	Yes ☐	No ☐
15. Internal Capsule	Yes ☐	No ☐
16. Thalamus	Yes ☐	No ☐
17. Cerebellum	Yes ☐	No ☐
18. Brainstem	Yes ☐	No ☐
i) Pons	Yes ☐	No ☐
ii) Midbrain	Yes ☐	No ☐

14. TREATMENT BEFORE STROKE

1) Anti-Hypertensive:	Yes ☐	No ☐
a) Calcium Channel Blocker	Yes ☐	No ☐
b) ACE Inhibitor	Yes ☐	No ☐
c) Angiotensin Receptor Blocker (ARB)	Yes ☐	No ☐
d) Beta Blockers	Yes ☐	No ☐
e) Alpha Methyl Dopa	Yes ☐	No ☐
f) Diuretics	Yes ☐	No ☐
i) Potassium Sparing Diuretics	Yes ☐	No ☐
ii) Thiazide and Thiazide-like	Yes ☐	No ☐
iii) Loop Diuretics	Yes ☐	No ☐
g) Alpha 1 Adrenergic Blockers	Yes ☐	No ☐

II) Others:

a) Antiplatelet:	Yes ☐	No ☐	
If Yes;	**A) Aspirin**	**B) Clopidogrel**	**C) Dipyridamole**

b) Anticoagulant Yes ☐ No ☐

If Yes; **A) Warfarin** **B) Dabiatran** **C) Rivaroxaban** **D) Heparin**

c. Antidiabetic Yes ☐ No ☐

If Yes; A) Insulin B) Oral Hypoglycemia C) Dipyridamole

d. Antioxidant Yes ☐ No ☐

e. Physiotherapy Yes ☐ No ☐

f. Speech Therapy Yes ☐ No ☐

g. Statin Yes ☐ No ☐

h. Mannitol Yes ☐ No ☐

i. Steroids Yes ☐ No ☐

j. Antidepressant Yes ☐ No ☐

14. TREATMENT AFTER STROKE

1) Anti-Hypertensive:	Yes ☐	No ☐
a) Calcium Channel Blocker	Yes ☐	No ☐
b) ACE Inhibitor	Yes ☐	No ☐
c) Angiotensin Receptor Blocker (ARB)	Yes ☐	No ☐
d) Beta Blockers	Yes ☐	No ☐
e) Alpha Methyl Dopa	Yes ☐	No ☐
f) Diuretics	Yes ☐	No ☐
i) Potassium Sparing Diuretics	Yes ☐	No ☐
ii) Thiazide and Thiazide-like	Yes ☐	No ☐
iii) Loop Diuretics	Yes ☐	No ☐
g) Alpha 1 Adrenergic Blockers	Yes ☐	No ☐

II) Others:

a) Antiplatelet:	Yes ☐	No ☐		
If Yes;	**A) Aspirin**	**B) Clopidogrel**	**C) Dipyridamole**	
b) Anticoagulant	Yes ☐	No ☐		
If Yes;	**A) Warfarin**	**B) Dabiatran**	**C) Rivaroxaban**	**D) Heparin**
c. Antidiabetic	Yes ☐	No ☐		
If Yes;	A) Insulin	B) Oral Hypoglycemia	C) Dipyridamole	

d. Antioxidant	Yes ☐	No ☐
e. Physiotherapy	Yes ☐	No ☐
f. Speech Therapy	Yes ☐	No ☐
g. Statin	Yes ☐	No ☐

h. Mannitol	Yes ☐	No ☐
i. Steroids	Yes ☐	No ☐
j. Antidepressant	Yes ☐	No ☐

15. COMPLICATIONS:

Raised ICP	Yes	No
Aspiration Pneumonia	Yes	No
Deep Venous Trombosis	Yes	No
Arrytmias	Yes	No
Seizure disorder	Yes	No
PTE	Yes	No
UTI	Yes	No
Pressure Ulcers	Yes	No
Depression	Yes	No
Dementia	Yes	No
Parkinsonism	Yes	No

16. DISCHARED INFORMATION

Date of Admission_____

Date of Discharge _____

1. CLINICAL CHARACTERISTICS

	Presentation	24 hrs	72 hrs	7days	14days	1 month	3 months	6 months	9 months	12 months
NIHSS										
MRS										
BARTHEL INDEX										
Systolic blood pressure										
Diastolic blood pressure										

5. Vascular Risk Factors Assessment

Patient's Medical History

Have you been diagnosed with?

Hypertension Yes No Do not know Chronic kidney disease Yes No Do not know

Diabetes Mellitus Yes No Do not know Heart disease Yes No Do not know

Hyperlipidemia Yes No Do not know TIA Yes No Do not know

Stroke Yes No Do not know Cancer Yes No Do not know

Migraine Yes No Do not know HIV Yes No Do not know

Neck injury Yes No Do not know Obesity Yes No Do not know

Neck Manipulation Yes No Do not know TB Yes No Do not know

Recurret miscarriage Yes No Do not know Haemoglobinopathy Yes No Do not know

Sleep disorders Yes No Do not know Alcohol Yes No Do not know

Chronic bronchitis Yes No Do not know Bronchitis Yes No Do not know

Acute fibrile illness within the past Yes No Do not know Others (specify) ¬¬¬_____

4 wks

Any dental problem in the last one year? Yes No Do not know

Smoking Yes No Do not know

If Yes Painful teeth Yes No Do not know Painful gums Yes No Do not know

Stress in the last 2 weeks Yes No Do not know Lost teeth Yes No Do not know

Depression in the last 4 weeks Yes No Do not know

Use of OCP (for women) Yes No Do not know

	Presentation		24 Hours		72 Hours		14 Days		21 Days		1 months		3 months		6 months		9months		1 year	
Seizure	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No
Focal onset																				
Generalized onset																				
Focal to Bilateral tonic clonic																				
Unknown onset																				
Motor involvement																				

6. SEIZURE CHARACTERISTICS

16. EPILEPSY CHARACTERISTICS

A) None	B) Focal	C) Generalized	D) Combine	E) Unknown

17. MEDICATION

i) Carbamazepine	ii) Levetiracetam	iii) Phenobarbitone	iv) Sodium Vaporate
v) Oxcarbazepine	vi) Topiramate	vii) Phenytoin	viii) Gabapentin
ix) Lamotrigine	x) Not Applicable		

15. EEG CHARACTERISTICS

1. Background

a) Beta	b) Alpha	c) Theta	d) Delta	e) Intermixed Fast	f)Intermixed Slow

2. Frequency

a) Fast	b) Slow

3. Slowing

a) Nil	b) Generalized	c) Focal	f) Intermittent

4. Epileptiform

a) Nil	b) Focal	c) Generalized	f)Focal-Generalized

5.Periodic Pattern **Epileptiform** Yes ☐ No ☐

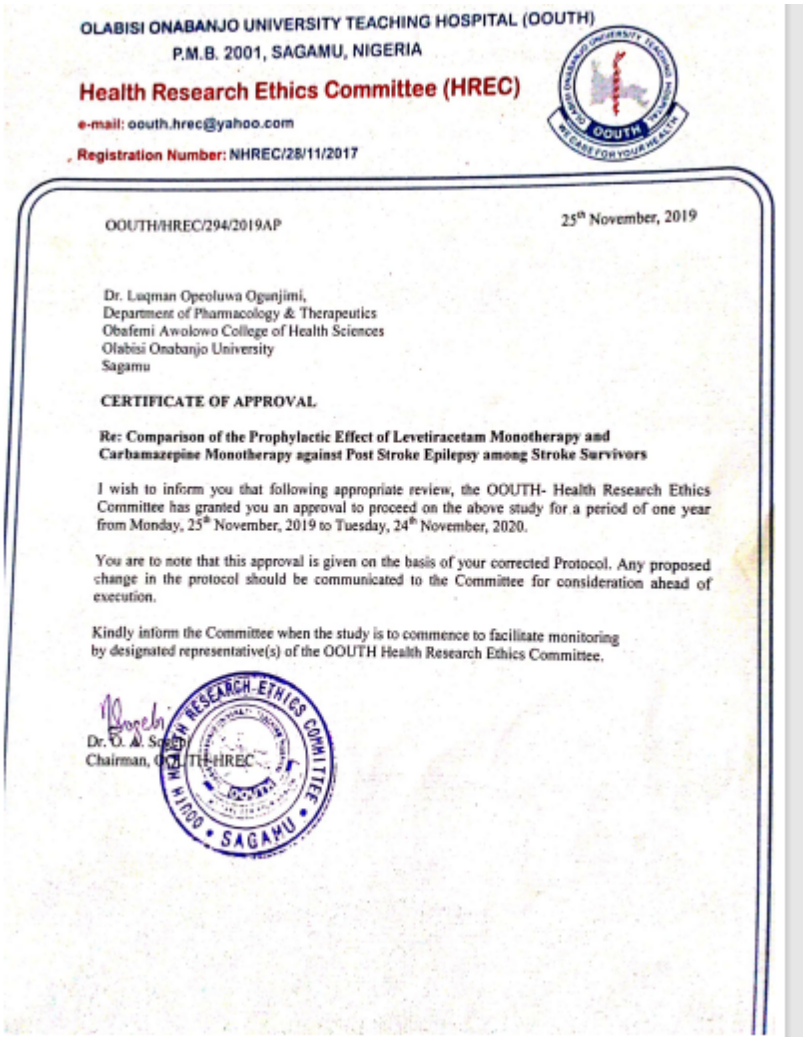
COGNITIVE SCREENING INSTRUMENT FOR DEMENTIA

	Score At 1 Month	Score At 3 Month	Score At 6 Month	Score At 9 Month	Score At 1 Year
LANGUAGE					
1. Language Expression					
Naming	/7	/7	/7	/7	/7
Definition	/5	/5	/5	/5	/5
Repetition	/1	/1	/1	/1	/1
Fluency	/5	/5	/5	/5	/5
Language Expression total score	/18	/18	/18	/18	/18
2. Language Comprehension	/5	/5	/5	/5	/5
3. Total Language Score	/23	/23	/23	/23	/23
B. Memory					
1. Registration	/4	/4	/4	/4	/4
2. Delayed Recall	/2	/2	/2	/2	/2
3. Memory Short Test (Immediate Recall)	/6	/6	/6	/6	/6
4. Semantic	/9	/9	/9	/9	/9
Total Memory Score	/21	/21	/21	/21	/21
C. Attention and Calculation	/8	/8	/8	/8	/8
D. Orientation					
Time	/4	/4	/4	/4	/4
Place	/6	/6	/6	/6	/6
Orientation Total Sore	/10	/10	/10	/10	/10
E.PRAXIS/Stick Design assessement					
1. Square	/3	/3	/3	/3	/3
2.Triangle with leg	/3	/3	/3	/3	/3

3. Chevron	/3	/3	/3	/3	/3
4. Rake	/3	/3	/3	/3	/3
PRAXIS TOTAL SCORE	/12	/12	/12	/12	/12
OVERALL TOTAL SCORE	/74	/74	/74	/74	/74

APPENDIX III

ETHICAL APPROVAL



OLABISI ONABANJO UNIVERSITY TEACHING HOSPITAL (OOUTH)
P.M.B. 2001, SAGAMU, NIGERIA

Health Research Ethics Committee (HREC)

e-mail: oouth.hrec@yahoo.com

Registration Number: NHREC/28/11/2017

OOUTH/HREC/294/2019AP

25th November, 2019

Dr. Luqman Opeoluwa Ogunjimi,
Department of Pharmacology & Therapeutics
Obafemi Awolowo College of Health Sciences
Olabisi Onabanjo University
Sagamu

CERTIFICATE OF APPROVAL

Re: Comparison of the Prophylactic Effect of Levetiracetam Monotherapy and Carbamazepine Monotherapy against Post Stroke Epilepsy among Stroke Survivors

I wish to inform you that following appropriate review, the OOUTH- Health Research Ethics Committee has granted you an approval to proceed on the above study for a period of one year from Monday, 25th November, 2019 to Tuesday, 24th November, 2020.

You are to note that this approval is given on the basis of your corrected Protocol. Any proposed change in the protocol should be communicated to the Committee for consideration ahead of execution.

Kindly inform the Committee when the study is to commence to facilitate monitoring by designated representative(s) of the OOUTH Health Research Ethics Committee.

Dr. O. A. Soseb
Chairman, OOUTH-HREC

OOUTH HEALTH RESEARCH ETHICS COMMITTEE SAGAMU

APPENDIX IIIB

ETHICAL APPROVAL

OLABISI ONABANJO UNIVERSITY TEACHING HOSPITAL (OOUTH)
P.M.B. 2001, SAGAMU, NIGERIA
Health Research Ethics Committee (HREC)
e-mail: oouth.hrec@yahoo.com
Registration Number: NHREC/28/11/2017

OOUTH/HREC/275/2019AP

25th November, 2019

Dr. Luqman Opeoluwa Ogunjimi,
Department of Pharmacology & Therapeutics
Obafemi Awolowo College of Health Sciences
Olabisi Onabanjo University
Sagamu

CERTIFICATE OF APPROVAL

Re: Clinical Profile and Predictors of Post Stroke Seizures and Epilepsy

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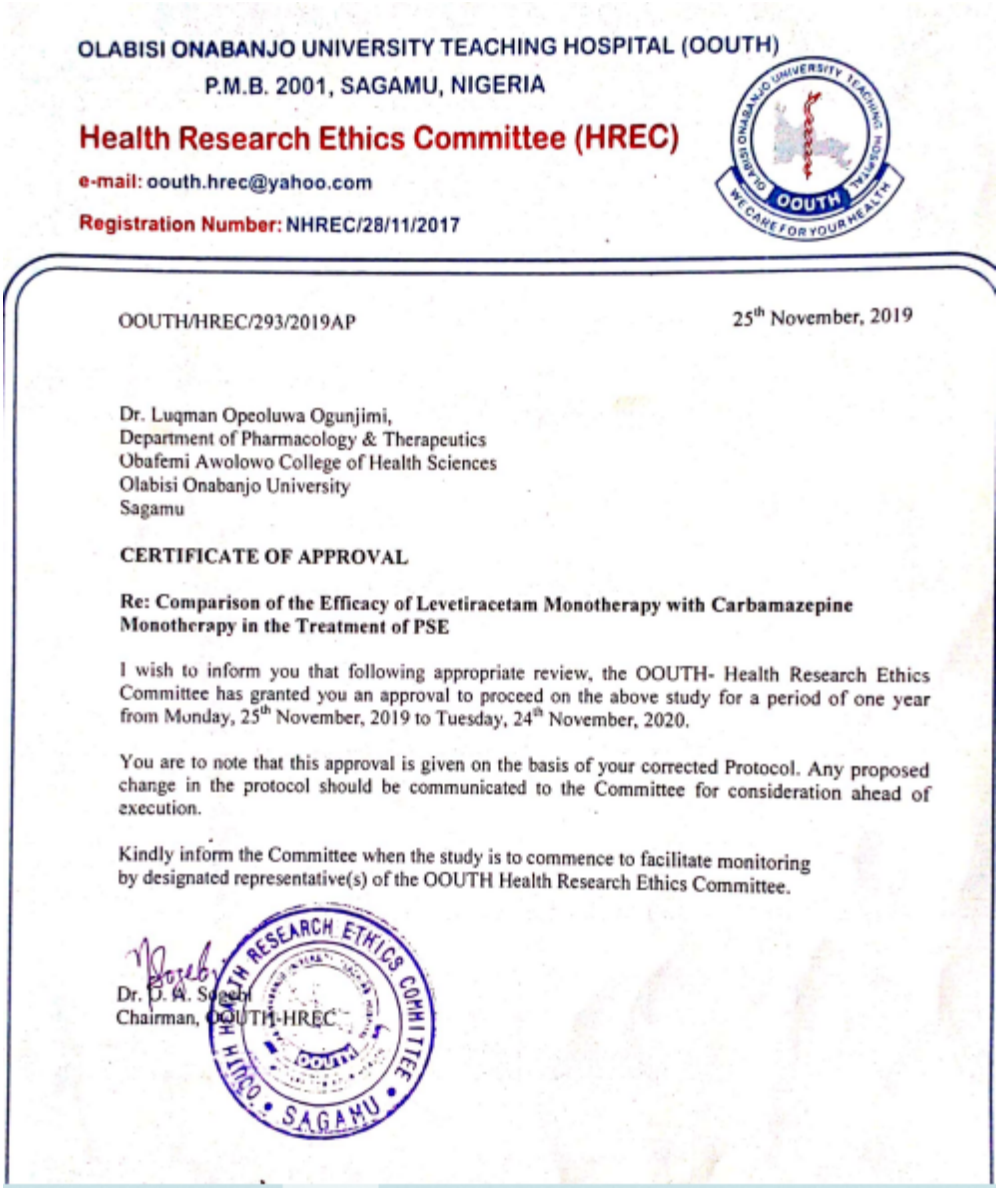
Dr. O. A. Sogebi
Chairman, OOUTH-HREC

OOUTH HEALTH RESEARCH ETHICS COMMITTEE • SAGAMU •

APPENDIX IIIC

ETHICAL APPROVALS



OLABISI ONABANJO UNIVERSITY TEACHING HOSPITAL (OOUTH)

P.M.B. 2001, SAGAMU, NIGERIA

Health Research Ethics Committee (HREC)

e-mail: oouth.hrec@yahoo.com

Registration Number: NHREC/28/11/2017

OOUTH/HREC/293/2019AP

25th November, 2019

Dr. Luqman Opeoluwa Ogunjimi,
Department of Pharmacology & Therapeutics
Obafemi Awolowo College of Health Sciences
Olabisi Onabanjo University
Sagamu

CERTIFICATE OF APPROVAL

Re: Comparison of the Efficacy of Levetiracetam Monotherapy with Carbamazepine Monotherapy in the Treatment of PSE

I wish to inform you that following appropriate review, the OOUTH- Health Research Ethics Committee has granted you an approval to proceed on the above study for a period of one year from Monday, 25th November, 2019 to Tuesday, 24th November, 2020.

You are to note that this approval is given on the basis of your corrected Protocol. Any proposed change in the protocol should be communicated to the Committee for consideration ahead of execution.

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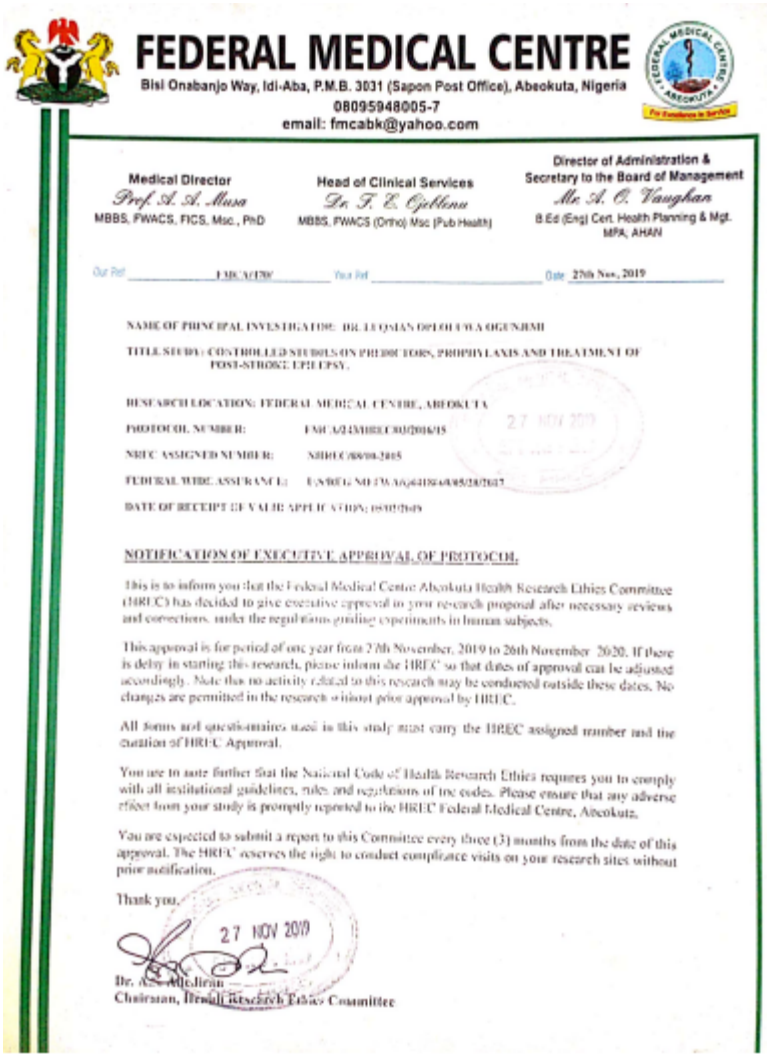
Dr. O. A. Sogeh
Chairman, OOUTH-HREC

OOUTH HEALTH RESEARCH ETHICS COMMITTEE • SAGAMU •

APPENDIX IIID

ETHICAL APPROVAL



FEDERAL MEDICAL CENTRE

Bisi Onabanjo Way, Idi-Aba, P.M.B. 3031 (Sapon Post Office), Abeokuta, Nigeria
08095948005-7
email: fmcabk@yahoo.com

Medical Director	Head of Clinical Services	Director of Administration & Secretary to the Board of Management
Prof. A. A. Musa	Dr. F. E. Ojelkun	Mr. A. O. Vaughan
MBBS, FWACS, FICS, Msc., PhD	MBBS, FWACS (Ortho) Msc (Pub Health)	B.Ed (Eng) Cert. Health Planning & Mgt. MPA, AHAN

Our Ref: FMC/A/1787 Your Ref: Date: 27th Nov., 2019

NAME OF PRINCIPAL INVESTIGATOR: DR. LUQMAN OPEOLUWA OGUNJIMI

TITLE STUDY: CONTROLLED STUDIES ON PREDICTORS, PROPHYLAXIS AND TREATMENT OF POST-STROKE EPILEPSY.

RESEARCH LOCATION: FEDERAL MEDICAL CENTRE, ABEOKUTA

PROTOCOL NUMBER: FMC/A/2143/HREC/03/2018/15

NHREC ASSIGNED NUMBER: NHREC/08/08/2015

FEDERAL WIDE ASSURANCE: FWA/IRB NO FWA00041834/IRB00017017

DATE OF RECEIPT OF VALID APPLICATION: 16/07/2019

NOTIFICATION OF EXECUTIVE APPROVAL OF PROTOCOL

This is to inform you that the Federal Medical Centre Abeokuta Health Research Ethics Committee (HREC) has decided to give executive approval to your research proposal after necessary reviews and corrections, under the regulations guiding experiments in human subjects.

This approval is for period of one year from 27th November, 2019 to 26th November 2020. If there is delay in starting this research, please inform the HREC so that dates of approval can be adjusted accordingly. Note that no activity related to this research may be conducted outside these dates. No changes are permitted in the research without prior approval by HREC.

All forms and questionnaires used in this study must carry the HREC assigned number and the duration of HREC Approval.

You are to note further that the National Code of Health Research Ethics requires you to comply with all institutional guidelines, rules and regulations of the codes. Please ensure that any adverse effect from your study is promptly reported to the HREC Federal Medical Centre, Abeokuta.

You are expected to submit a report to this Committee every three (3) months from the date of this approval. The HREC reserves the right to conduct compliance visits on your research sites without prior notification.

Thank you.

27 NOV 2019

Dr. A. S. Alkaliran
Chairman, Health Research Ethics Committee

APPENDIX IV

SAMPLES OF ELECTROENCEPHALOGRAPHY

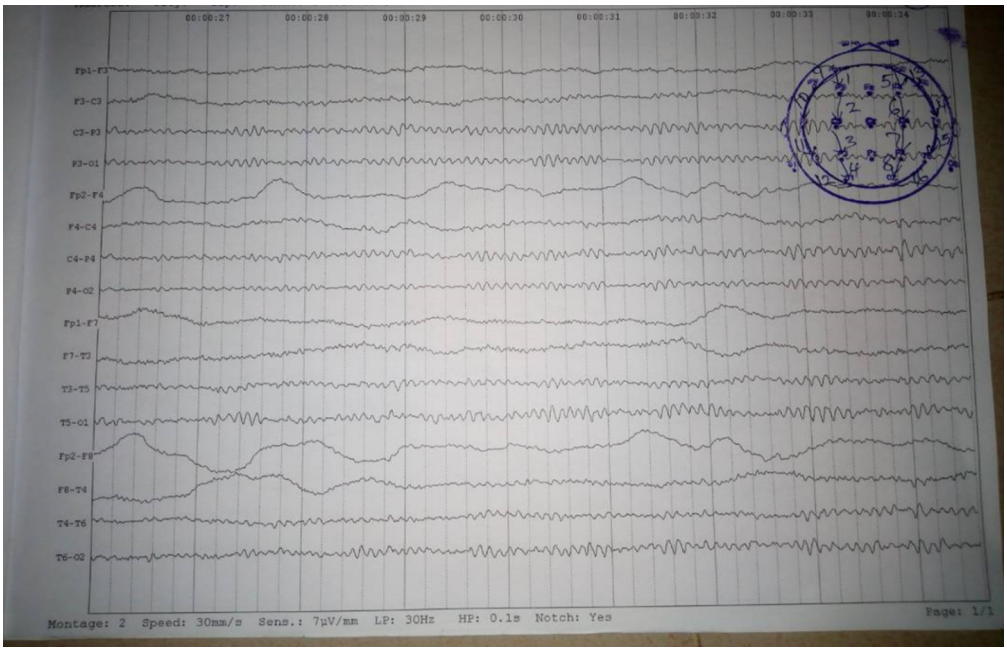


Plate I: Normal EEG with alpha background

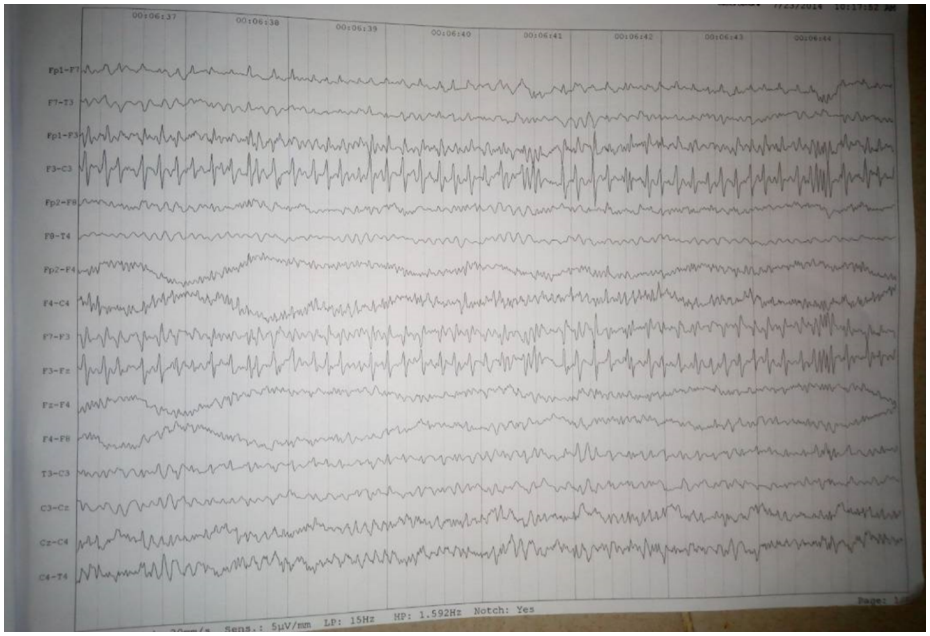


Plate II: Focal epileptiform discharges on EEG

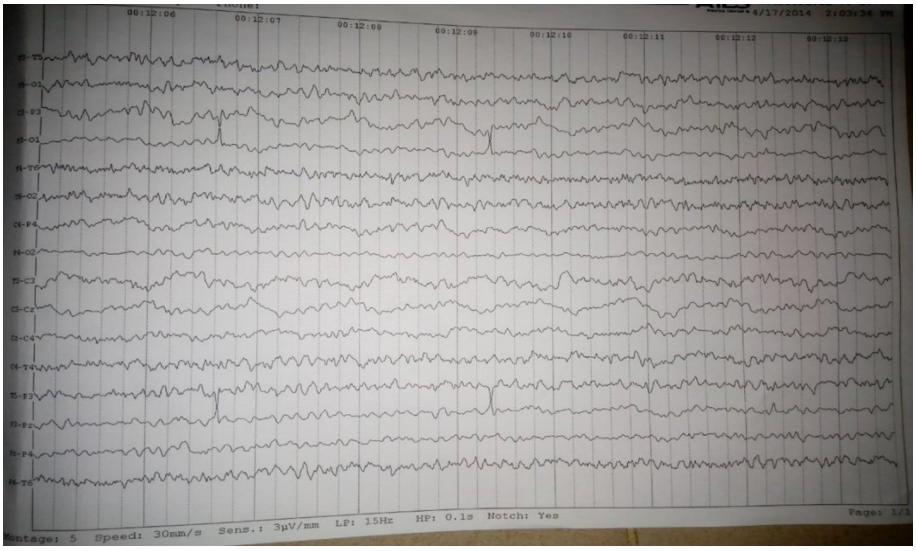


Plate III: Focal epileptiform discharges on EEG

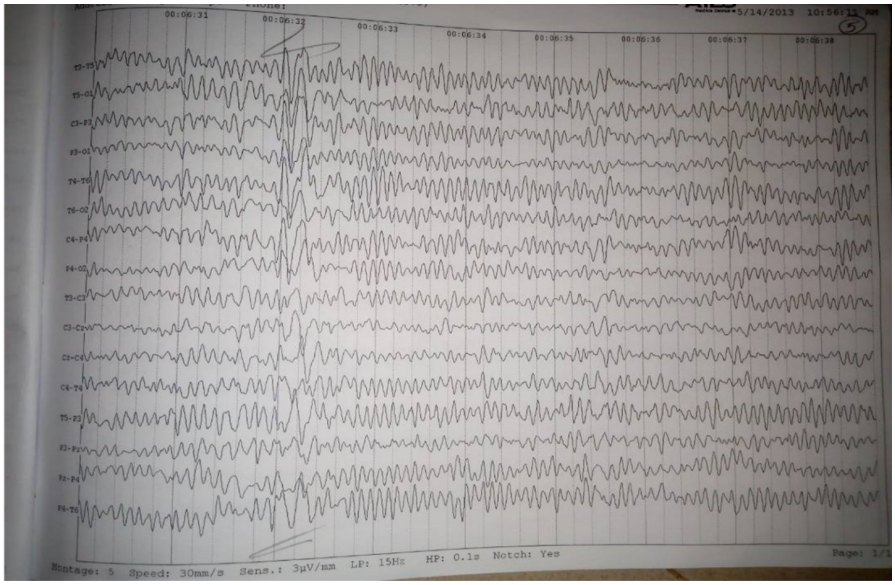


Plate V: Generalized epileptiform discharges on EEG

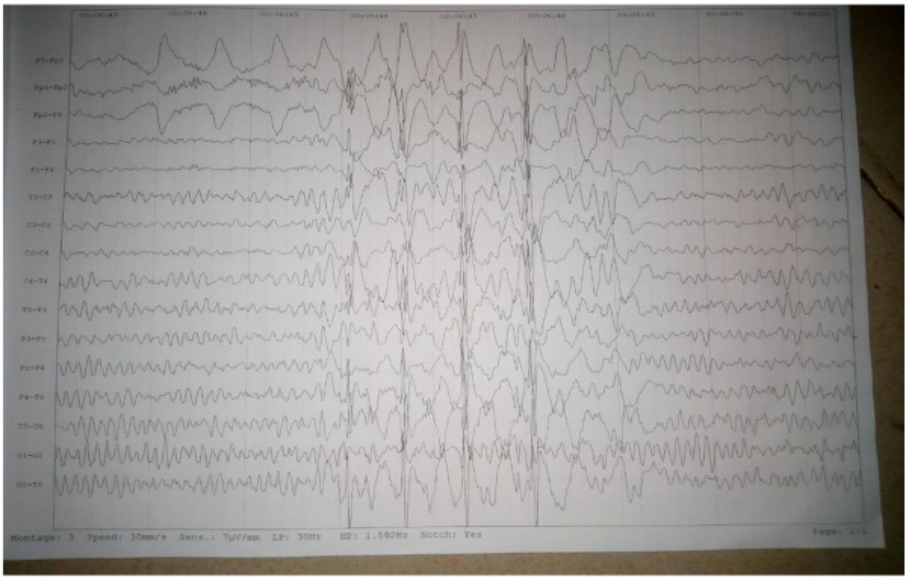


Plate V: Generalized epileptiform discharges on EEG

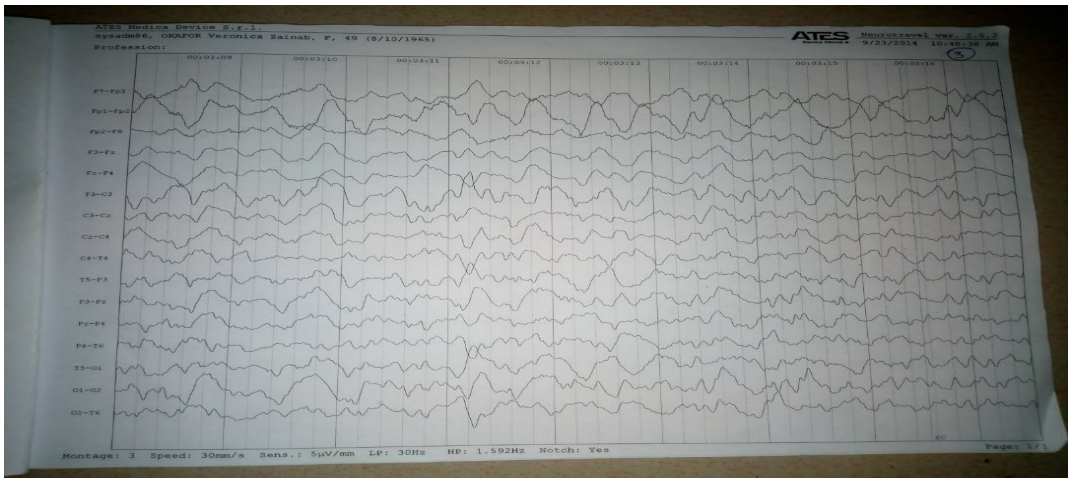


Plate VI: Generalized slowing on EEG

APPENDIX V

SAMPLES OF CRANIAL COMPUTED TOMOGRAPHY AND BRAIN MAGNETIC RESONANCE IMAGING

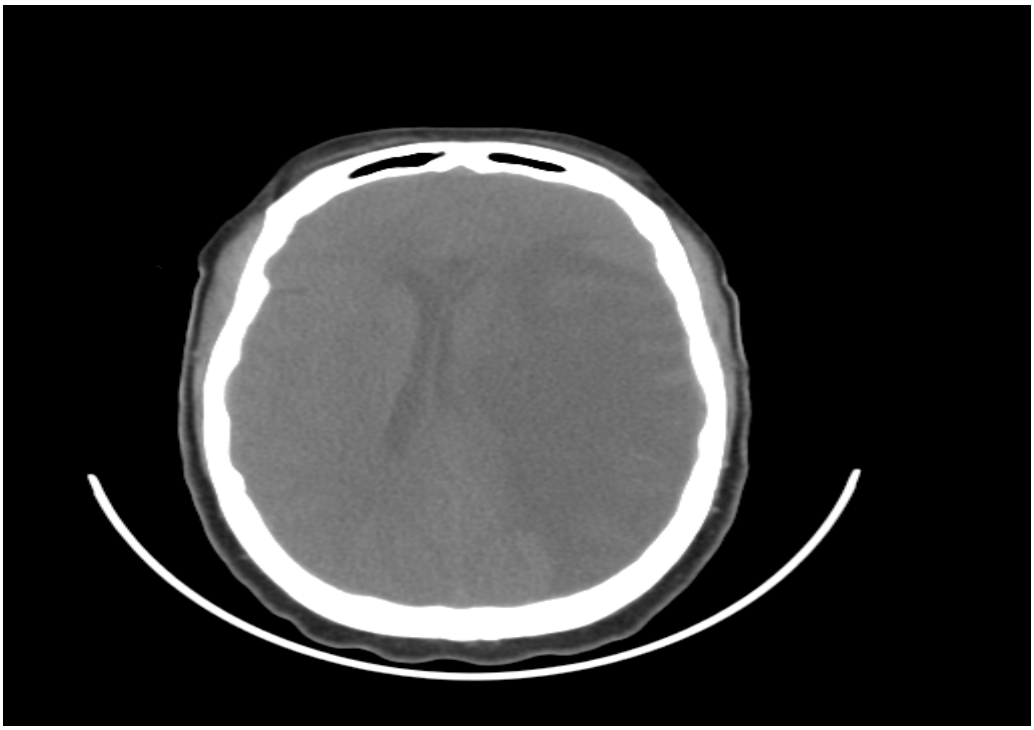


Plate VII: Brain CT of an extensive hypointensity in Middle Cerebral Artery with cortical involvement

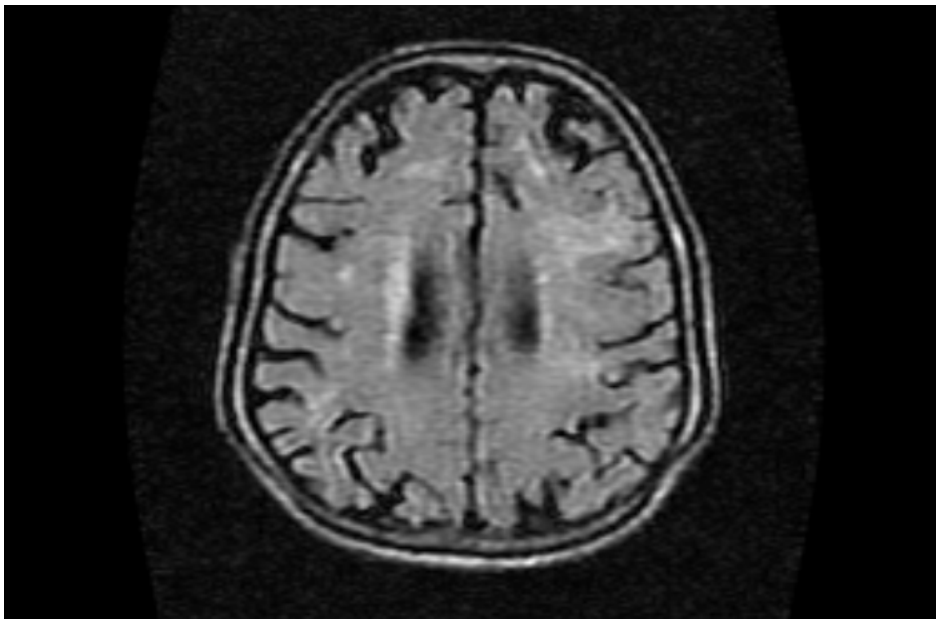


Plate VIII: Multiple lacunar infarct and periventricular white matter changes on flair sector of MRI

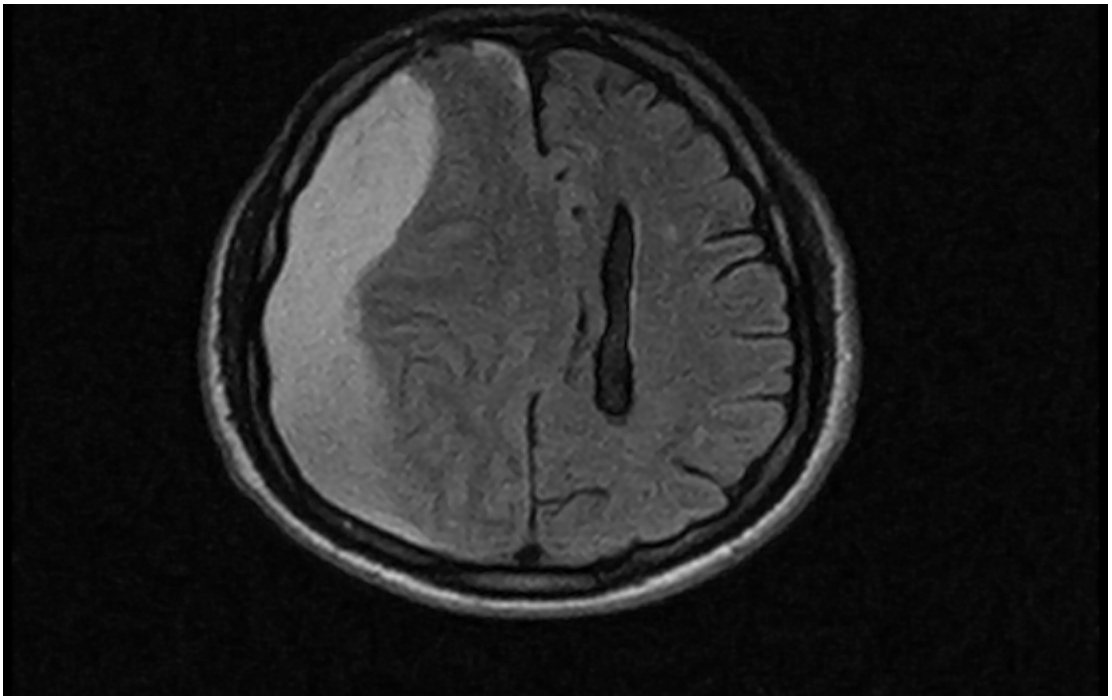


Plate IX: Subdural hematoma on MRI

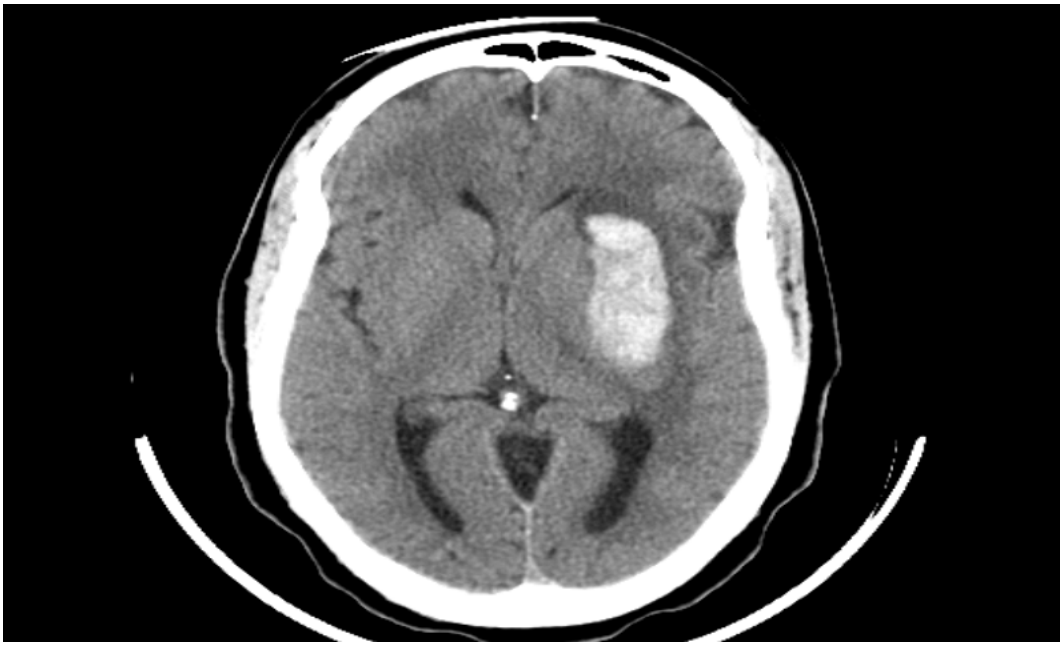


Plate X: A putaminal bleed

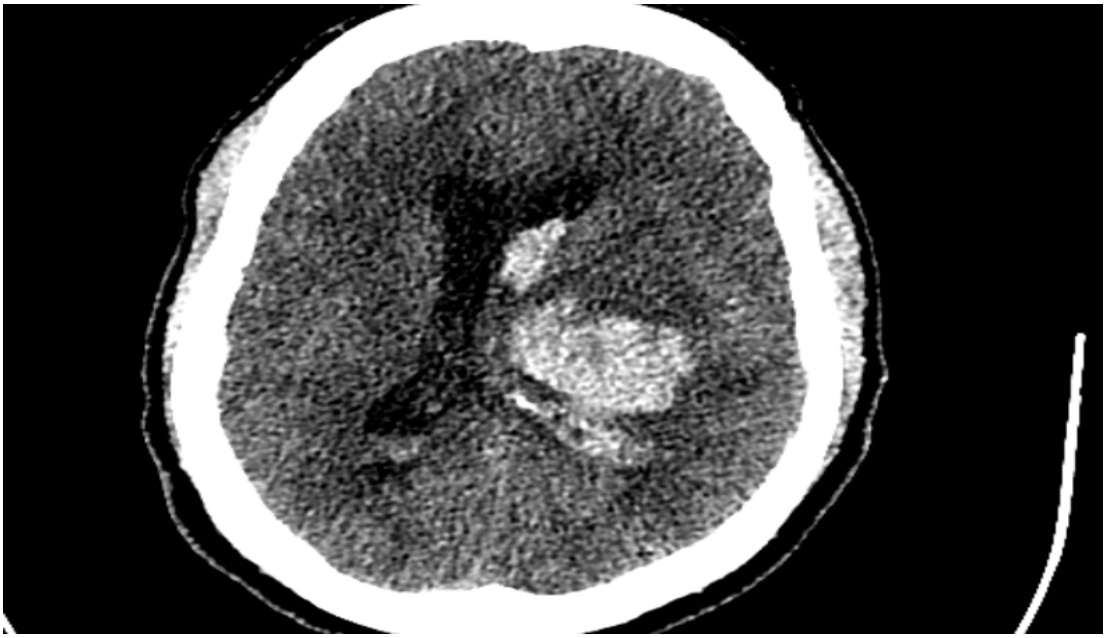


Plate xi: An extensive hyperintensity in thalomoganglionic area with mass effect

APPENDIC VI

FEDERAL MEDICAL CENTER ABEOKUTA

4.32 Socio-biological Characteristics of 140 Stroke Patients with Stroke Induced Seizure and Stroke Induced Epilepsy Treated at Federal Medical Centre Abeokuta for a period of two years

Of the 140 stroke patients recruited from FMCA, 88(62.9%) were males while 52(37.1%) were females. A total of 101(72%) had ischemic stroke while 39(28%) had hemorrhagic stroke. A total of 41(29%) developed seizure disorder following stroke. Of the 101 participants with ischemic stroke, 27(27%) developed seizures whereas seizure was recorded among 14 of the 39 individuals who had hemorrhagic stroke, (27% vs 36%).

Furthermore, 99(70.7%) of the participants had no seizure, of the 41 patients that developed seizure 14(10%), 14(10%), and 13(9.3%) had seizures only, seizure to epilepsy and epilepsy only respectively.

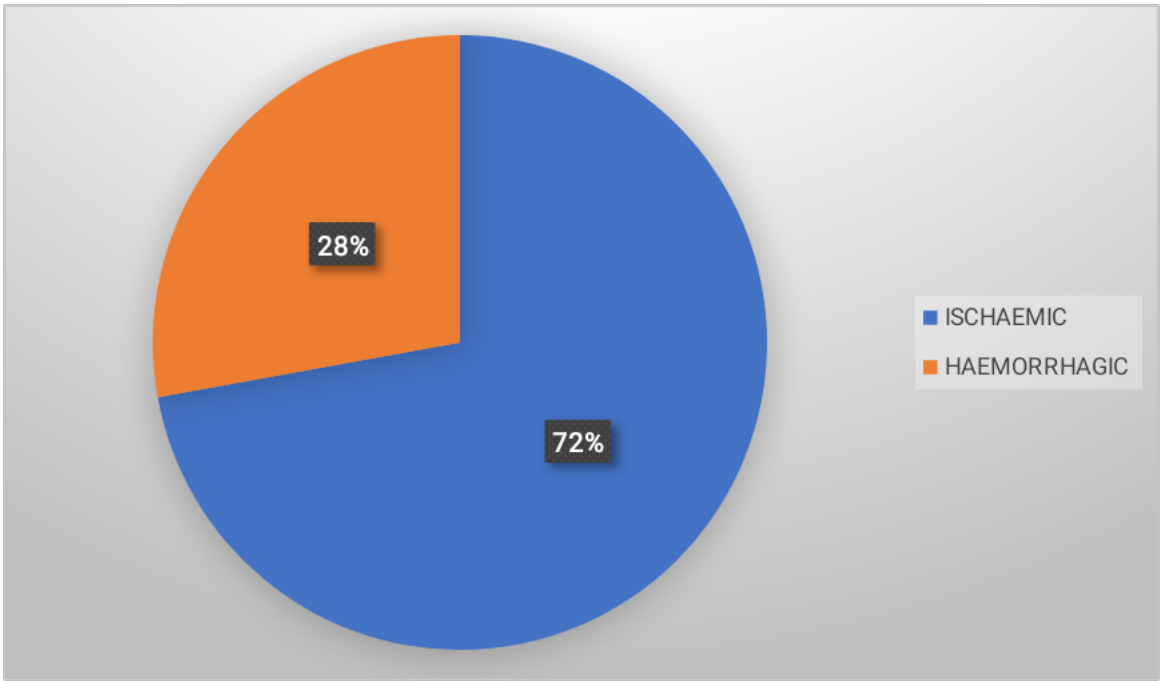


Figure 15: Stroke classification based on type among 140 cohorts Treated at Federal Medical Centre Abeokuta in South Western Nigeria for a period of two years

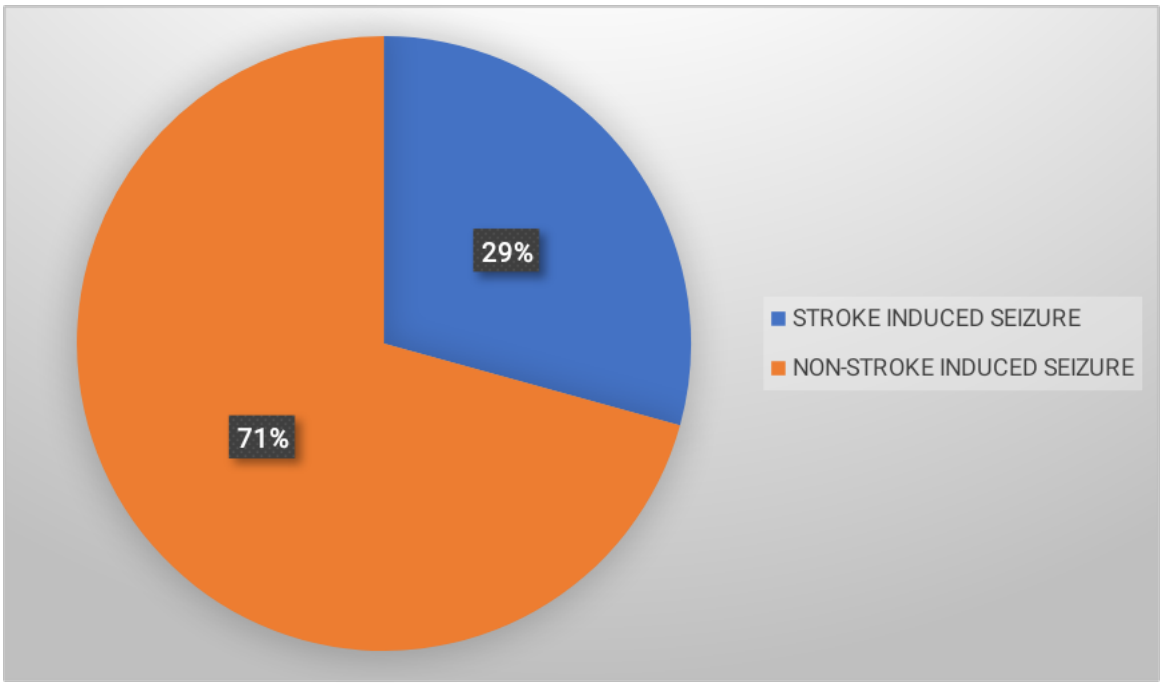


Figure 4.16: Stroke classification based on Seizure Occurrence/presence of Seizure among Post-Stroke Seizure and NSIS Patients Treated at Federal Medical Centre Abeokuta in South Western Nigeria for a period of two years

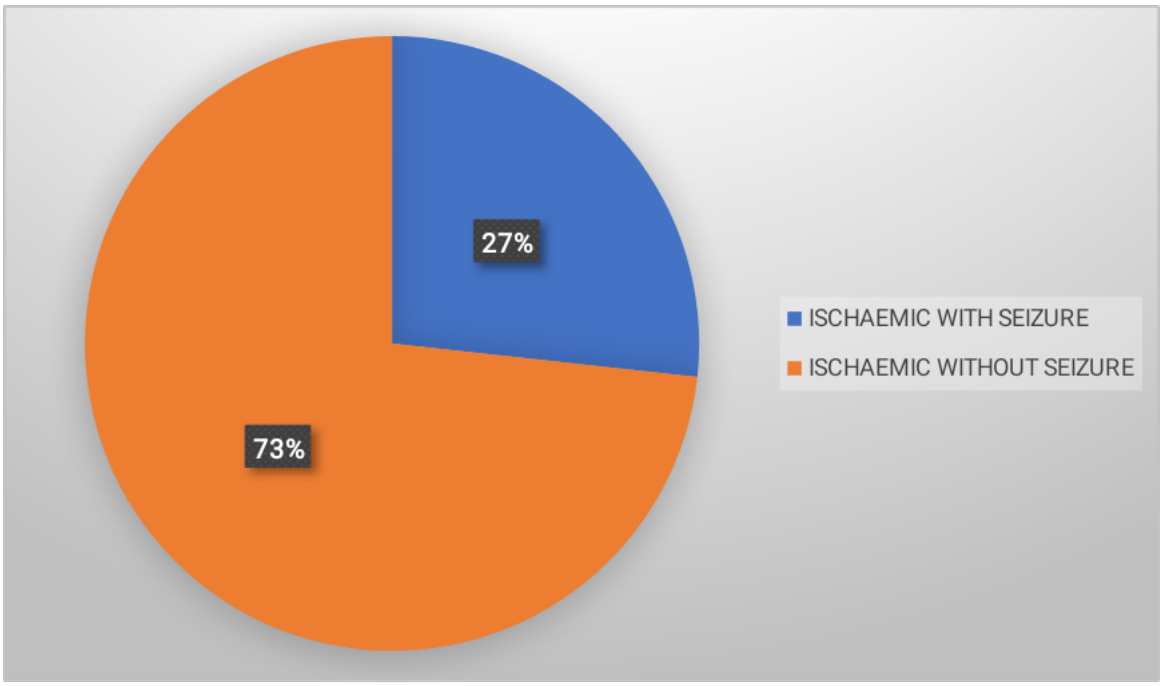


Figure 4.17: The Frequency of Haemorrhagic Stroke Participants with Stroke Induced Seizure and Non-Stroke Induced Seizure Treated at Federal Medical Centre Abeokuta in South Western Nigeria for a period of two years

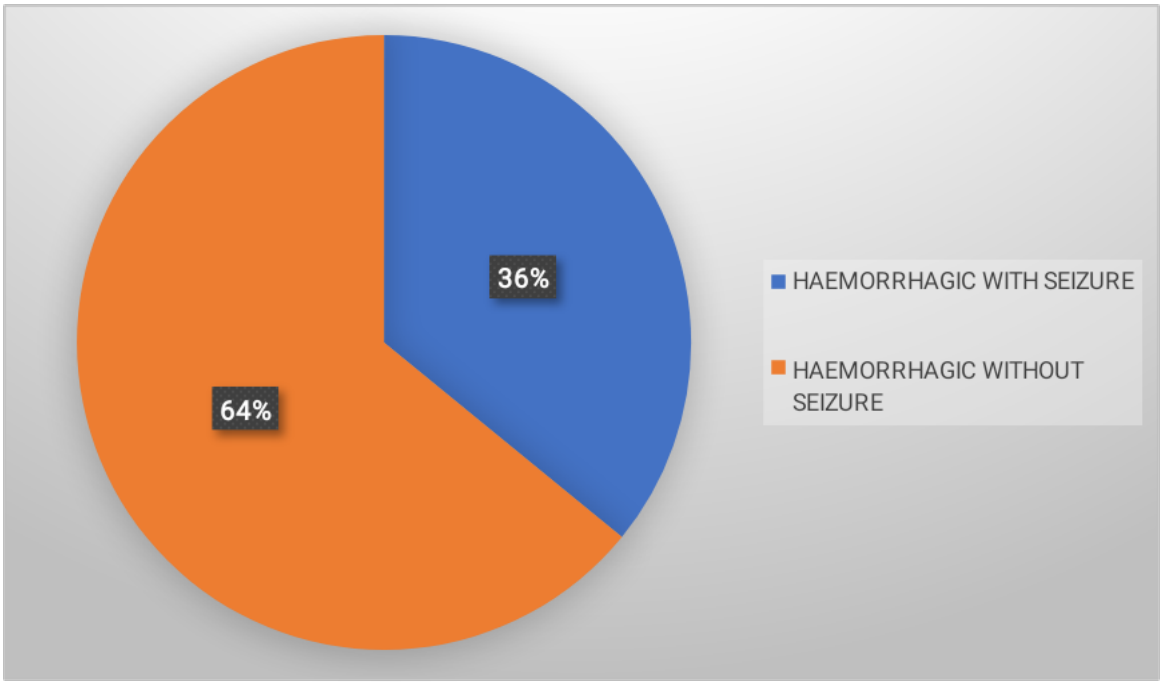


Figure 4.18: The Frequency of Ischaemic Stroke Participants with Stroke Induced Seizure and Non-Stroke Induced Seizure Treated at Federal Medical Centre Abeokuta in South Western Nigeria for a period of two years

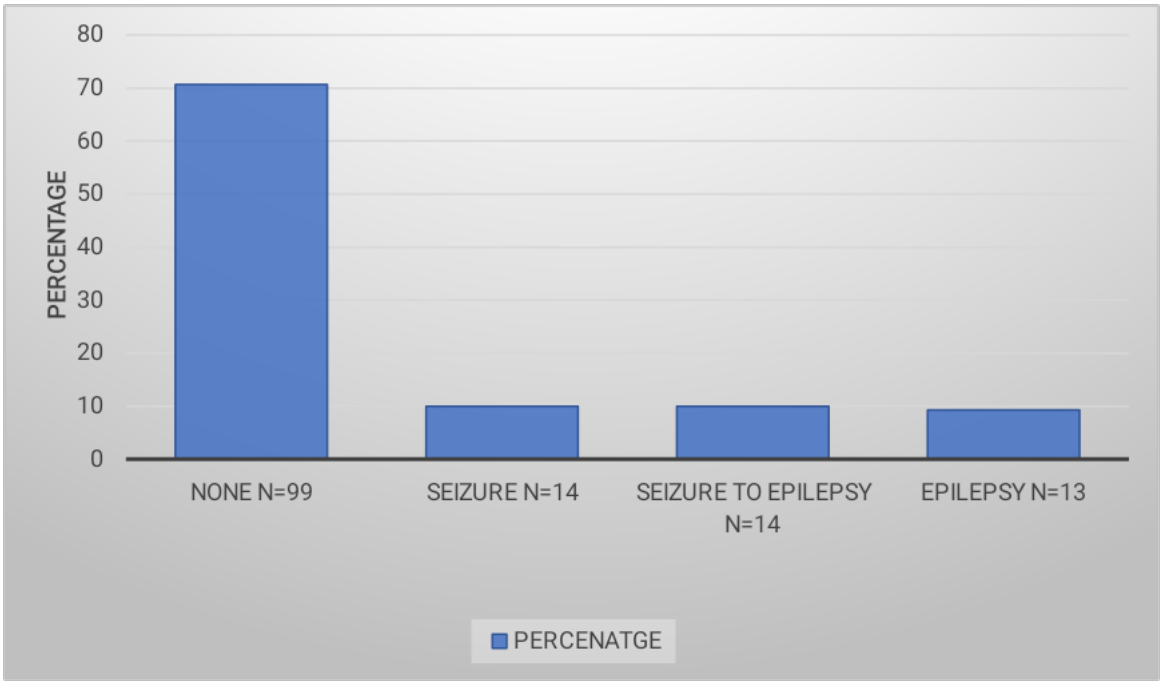


Figure 4.19: Frequency of Seizure and Epilepsy among Stroke Patients Treated at Federal Medical Centre Abeokuta in South Western Nigeria for a period of two years.

4.33 Comparison of Clinical characteristics of Stroke Survivors with or without Seizure treated at Federal Medical Centre, Abeokuta (FMCA) for a period of two years.

Patterns of stroke location revealed that there were higher number of participants with ischemic stroke at frontal lobe [46(45.5%) vs 7(17.9%); p ≤0.003], parietal lobe [59(58.4%) vs 3(7.7%); p <0.001], and lower number of participants at internal capsule [6(6.1%) vs 7(18.9%); p ≤0.023] and thalamus [6(5.9%) vs 13(33.3%); p <0.001] respectively compared to haemorrhagic stroke.

Majority of the participants had stroke in the MCA region with 73(72.3%) as ischemic and 14(35.9%) as haemorrhagic (p <0.001). Among participants with PCA, 10(9.9%) were ischaemic while 20(51.3%) were haemorrhagic stroke (p <0.001).

The use of antihypertensives was seen among 54(53.5%) ischaemic stroke cohort and 29(74.4%) among haemorrhagic stroke cohort and this was statistically significant (p ≤0.024). The median stroke size was 6.16±6.73 among ischaemic stroke cohort and 10.43±6.81 among haemorrhagic stroke cohort which is statistically significant (p ≤0.001).

Table 4.36: Comparison of Clinical characteristics among 346 Participants with Ischaemic and Haemorrhagic Treated at Federal Medical Centre Abeokuta in South Western Nigeria for a period of two years

Variables	Ischaemic n= 101	Haemorrhagic n = 39	Total N=140	x^2 Value	p Value
A. Clinical Characteristics					
Gender n (%) Male Female	 63(62.4) 38(37.6)	 25(64.1) 14(35.9)	 88(62.9) 52(37.1)	0.036	0.850
NIHSS at Presentation Mean±SD	17.76±10.19	21.03±9.61		-1.725	0.087
Stroke Severity n (%) Minor stroke Moderate stroke Moderate to severe Severe stroke	 14(14.3) 29(29.6) 13(13.3) 42(42.9)	 1(2.7) 11(29.7) 9(24.3) 16(43.2)	 15(11.1) 40(29.6) 22(16.3) 58(43.0)	5.260	0.154
Stroke size median (range)	6.16±6.73	10.43±6.81		-3.349	0.001 *
Hypertensive n(%) Anti-hypertensive n(%)	69(70.4) 54(53.5)	35(89.7) 29(74.4)	104(75.9) 83(59.3)	5.704 5.088	0.017 * 0.024 *
Diabetics n(%) Anti-diabetics n(%)	19(19.4) 14(13.9)	7(17.9) 2(5.1)	26(19.0) 16(11.4)	0.038 2.120	0.846 0.145
Statin n(%)	44(43.6)	9(23.1)	53(37.9)	5.020	0.025 *
Mass effect n(%)	7(6.9)	26(66.7)	33(23.6)	55.730	0.000 *
Large artery	31(30.7)	2(100.0)	33(32.0)	4.326	0.038

atherosclerosis n(%)					*
Raised ICP n(%)	22(21.8)	14(35.9)	36(25.7)	2.935	0.087
Aspiration pneumonia n(%)	20(19.8)	5(12.8)	25(17.9)	0.935	0.334
PTE n(%)	6(5.9)	0(0.0)	6(4.3)	2.421	0.120
B. Location					
Basal ganglia n(%) Caudate Lentiform	 3(3.0) 6(5.9)	 2(5.1) 9(23.1)	 5(3.6) 15(10.7)	 0.380 8.637	 0.537 0.003 *
Lobar Involvement n(%) Frontal Lobe Parietal Lobe Temporal Lobe Occipital Lobe	 46(45.5) 59(58.4) 17(17.0) 8(7.9)	 7(17.9) 3(7.7) 2(5.1) 3(7.7)	 53(37.9) 62(44.3) 19(13.7) 11(7.9)	 9.108 29.339 3.351 0.002	 0.003 * 0.000 * 0.067 0.964
Subcortical n(%) Internal Capsule Thalamus	 6(6.1) 6(5.9)	 7(18.9) 13(33.3)	 13(9.6) 19(13.6)	 5.151 17.999	 0.023 * 0.000 *
Infratentorial n(%) Cerebellum Brain stem Pons Midbrain	 5(5.0) 6(5.9) 6(5.9)	 2(5.1) 1(2.6) 1(2.6)	 7(5.0) 7(5.0) 7(5.0)	 0.002 0.675 0.675	 0.966 0.411 0.411
Cortical Involvement n(%) Cortical No cortical	 26(25.7) 75(74.3)	 6(15.4) 33(84.6)	 32(22.9) 108(77.1)	 1.712	 0.191

Age grouped 36-70 71-95	 74(73.3) 27(26.7)	 33(84.6) 6(15.4)	 107(76.4) 33(23.6)	2.101	0.156
C. Arterial Territory					
ACA n(%) MCA n(%) PCA n(%)	19(18.8) 73(72.3) 10(9.9)	5(12.8) 14(35.9) 20(51.3)	24(17.1) 87(62.1) 30(21.4)	0.711 15.828 28.616	0.399 0.000 * 0.000 *

NIHSS – National Institute of Health Stroke Scale Score PTE: Pulmonary Thromboembolism, ICP: Intracranial Pressure, ACA: Anterior Cerebral Artery, MCA: Middle Cerebral Artery, PCA: Posterior Cerebral Artery, *p<0.05 comparing ischaemic and haemorrhagic

4.34 Mortality Rate Among 140 Participants Treated at Federal Medical Centre, Abeokuta (FMCA) for a period of two years.

The mortality rate among stroke cohort was 12.1%, 29.3%, 29.3%, 32.9%, 34.3%, and 36.4% at 7 days, 1 month, 3 months, 6 months, 12 months, and 24 months, respectively. Furthermore, mortality rate was higher among hemorrhagic stroke cohort compared to ischemic stroke cohort from 7 days to 24 months and these were consistently statistically significant.

Table 37: Mortality Rate Among 140 Participants Treated at Federal Medical Centre, Abeokuta (FMCA) for a period of two years.

Variables	7days	1months	3months	6months	12months	24months
Stroke Patient n(%)	17(12.1)	41(29.3)	41(29.3)	46(32.9)	48(34.3)	51(36.4)
Ischaemic n(%)	9(8.9)	25(24.8)	25(24.8)	27(26.1)	29(28.7)	32(31.7)
Haemorrhagic n(%)	8(20.5)	16(41.0)	16(41.0)	19(48.7)	19(48.7)	19(48.7)
SIS n(%)	6(14.6)	14(34.1)	14(34.1)	16(39.0)	16(39.0)	17(41.5)
Seizure type						
ISPWS n(%)	1(3.7)	6(22.2)	6922.2)	7(25.9)	7(25.9)	8(29.6)
HSPWS n(%)	5(35.7)	8(57.1)	8(57.1)	9(64.3)	9(64.0)	9(64.0)

SIS – Stroke Induced Seizures ISCH- Ischaemic Stroke Patients with Seizures HSPWS Haemorrhagic Stroke Patients with Seizures

4.35: Comparison of Sociodemographic Clinical Characteristics among 27 Ischaemic Stroke Patients and 14 Haemorrhagic Stroke Patients with Stroke Induced Epilepsy

Among 41 patients that developed SIE, 25(61%) were males and 16(39%) were females. There were 27(65.9%) ischemic and 14(34.1%) haemorrhagic stroke participants that developed SIE. The mean age of participants with SIE among ischemic stroke patients is 67.41±11.96 compared to a value of 57.29±12.15 among haemorrhagic stroke patient with SIE and this attained a significant level (p ≤0.015). The mean stroke volume among participants with ischaemic stroke with SIE is 18.17(12.90) compared to the value of 27.29(10.16) among those with haemorrhagic stroke with SIE and this was significant (p≤0.027).

Of the 27(65.9%) with MCA stroke with SIE, majority 21(77.8%) were ischemic compared to 6(42.9%) of haemorrhagic stroke patients which was statistically significant (p≤0.025). Among those with PCA stroke with SIE, 0(0.0%) were ischaemic compared to 6(42.9%) that had haemorrhagic stroke, and this was significant (p≤0.001). Among the 41 patients with SIE, the frequency of statin usage was 19(70.4%) among ischemic cohorts compared to 3(21.4%) among haemorrhagic stroke patients and this was significant (p≤0.003).

Furthermore, the presence of mass effect was more among haemorrhagic cohorts 8(57.1%) compared to 3(11.1%) among ischaemic cohorts (p≤0.002).

Table 38: Comparison of Sociodemographic Clinical Characteristics among 27 Ischaemic Stroke Patients and 14 Haemorrhagic Stroke Patients with Stroke Induced Epilepsy

Variables	ISPWS n=27	HMPWS n=14	x^2 value	p value
Gender n(%) Male Female	 17(63.0) 10(37.0)	 8(57.1) 6(42.9)	 0.131	 0.717
Age Mean (SD)	67.41±11.96	57.29±12.15	2.556	0.015
Stroke size Median (Range)	7.26(6.29)	11.21(9.00)	-1.645	0.108
Stroke volume cm^3 Median (Range)	18.17(12.90)	27.29(10.16)	-2.297	0.027*
Cortical involvement n(%) Cortical No cortical	 12(44.4) 15(55.6)	 4(28.6) 10(71.4)	 0.976	 0.323
Hypertensive n(%)	17(70.8)	14(100.0)	5.005	0.025*
Diabetics n(%)	7(29.2)	3(21.4)	0.273	0.601
ACA n(%)	6(22.2)	2(14.3)	0.370	0.543
MCA n(%)	21(77.8)	6(42.9)	5.000	0.025*
PCA n(%)	0(0.0)	6(42.9)	13.555	<0.001*
Antihypertensive n(%)	19(70.4)	11(78.6)	0.326	0.574
Anti-diabetics n(%)	5(18.5)	1(7.1)	0.955	0.328
Statin n(%)	19(70.4)	3(21.4)	8.881	0.003*
Mass effect n(%)	3(11.1)	8(57.1)	9.951	0.002*
Large artery atherosclerosis n(%)	10(37.0)	2(100.0)	3.043	0.081

ACA: Anterior Cerebral Artery, MCA: Middle Cerebral Artery, PCA: Posterior Cerebral Artery, PTE: Pulmonary Thromboembolism, UTI: Urinary Tract Infection, ICP: Intracranial Pressure, ISPWS: Ischaemic Stroke Patients with Seizures, HSPWS: Haemorrhagic Stroke Patients with Seizures, *p<0.05 comparing ISPWS and HMPWS

4.36 Comparison of Socio-biological Characteristics between Participants with Ischemic Stroke with or without seizure treated at Federal Medical Centre, Abeokuta over a period of two years.

Of the 101(72%) participants with ischemic stroke, 27(27%) had SIS/SIE with 17(63.0%) males and 10(37.0%) females. 19(70.4%) of ischemic SIS/SIE used antihypertensive while 35(47.3%) of ischemic NSIS used antihypertensive (p≤0.040). Concerning use of statin, 19(70.4%) of ischemic SIS/SIE used statin while 25(33.8%) of ischemic NSIS used statin (p≤0.001). Again, presence of cortical involvement of cranial CT was higher 12(44.4%) in the ischemic stroke patients with SIS/SIE compared to 14(18.9%) NSIE (p≤0.009). The mean age of ischemic stroke patients with SIS/SIE was 67.41±11.96 compared to 61.58±9.74 among ischemic cohort with NSIS and this was statistically significant (p≤0.014).

Furthermore, there was a significant difference between ischemic cohort with SIS/SIE and NSIS with regards to raised ICP (p≤0.025) and PTE (p≤0.023).

Table 39: Comparison of Socio-biological Characteristics between Participants with Ischemic Stroke with or without seizure treated at Federal Medical Centre, Abeokuta over a period of two years.

Variable n(%)	SIS/SIE n=27	NSIS n=74	Statistics	p-value
Gender Male Female	17(63.0) 10(37.0)	46(62.2) 28(37.8)	0.005	0.941
Mass effect	3(11.1)	4(5.4)	0.999	0.318
Antihypertensive	19(70.4)	35(47.3)	4.233	0.040*
Anti-diabetics	5(18.5)	9(12.2)	0.669	0.413
Statin	19(70.4)	25(33.8)	10.770	0.001*
Raised ICP	10(37.0)	12(16.2)	5.033	0.025*
Aspiration pneumonia	5(18.5)	15(20.3)	0.038	0.845
PTE	4(14.8)	2(2.7)	5.194	0.023*
UTI	6(22.2)	11(14.9)	0.765	0.382
Hypertension	17(70.8)	52(70.3)	0.003	0.958
Diabetes mellitus	7(29.2)	12(16.2)	1.945	0.163
Sleep disorder	3(12.5)	2(2.7)	3.593	0.058
Cortical involvement Cortical Not cortical	12(44.4) 15(55.6)	14(18.9) 60(81.1)	6.743	0.009*
ACA n(%)	6(22.2)	13(17.6)	0.281	0.596
MCA n(%)	21(77.8)	52(70.3)	0.556	0.456
PCA n(%)	0(0.0)	10(13.5)	4.050	0.044*
AGE Mean(SD)	67.41±11.96	61.58±9.74	2.499	0.014*
NIHSS 0 Mean(SD	18.59±10.49	17.46±10.1	0.493	0.623

		4		
Stroke size	6.00(29.00)	3.00(39.00)	0.999	0.325
Stroke volume	18.00(39.00)	6.00(59.00)	1.575	0.118

SIS: Stroke Induced Seizure Patients, NSIS: Non-Stroke Induced Seizures, ACA: Anterior Cerebral Artery, MCA: Middle Cerebral Artery, PCA: Posterior Cerebral Artery, IVH: Intraventricular Haemorrhage, NIHSS: National Institute Health Stroke Scale Score *p<0.05 comparing SIS/SIE and NSIS

Table 40: Comparison of Socio-biological Characteristics between Participants with Ischemic Stroke with or without seizure treated at Federal Medical Centre, Abeokuta over a period of two years.

Variable n(%)	SIS/SIE n=27(26.7)	NSIS n=74(73.3)	Statistics	p-value
Background Alpha Theta Delta Intermixed fast	 6(22.2) 12(44.4) 9(33.3) 0(0.0)	 26(35.1) 30(40.5) 17(23.0) 1(1.4)	2.303	0.512
Slowing Focal Generalized Intermittent No	 1(3.7) 10(37.0) 10(37.) 6(22.2)	 0(0.0) 17(23.0) 23(31.1) 34(45.9)	7.230	0.065

SIS: Stroke Induced Seizure, NSIS: Non-Stroke Induced Seizures

4.37: Comparison of Socio-biological Characteristics between participants with Hemorrhagic Stroke with or without Seizure treated at Federal Medical Centre, Abeokuta (FMCA) over the period of two years.

Of the 39 participants with hemorrhagic stroke, 14(36%) had SIS/SIE while 25(64%) had NSIS. Of the 14 hemorrhagic cohort with SIS/SIE, 8(57.1%) were males compared to 6(42.9%) females while hemorrhagic cohort with NSIS comprised 17(68.0%) males and 8(32.0%) females.

Table 41: Comparison of Socio-biological Characteristics between participants with Hemorrhagic Stroke with or without Seizure treated at Federal Medical Centre, Abeokuta (FMCA) over the period of two years.

Variable n(%)	SIS/SIE n=14	NSIS n=25	Statistics	p-value
Gender Male Female	8(57.1) 6(42.9)	17(68.0) 8(32.0)	0.460	0.498
Mass effect	8(57.1)	18(72.0)	0.891	0.345
Antihypertensive	11(78.6)	18(72.0)	0.203	0.652
Anti-diabetics	1(7.1)	1(4.0)	0.182	0.669
Statin	3(21.4)	6(24.0)	0.033	0.855
Raised ICP	5(35.7)	9(36.0)	0.000	0.986
Aspiration pneumonia	1(7.1)	4(16.0)	0.630	0.427
Hypertension	14(100.0)	21(84.0)	2.496	0.114
Diabetes mellitus	3(21.4)	4(16.0)	0.180	0.672
Cortical involvement Cortical Not cortical	4(28.6) 10(71.4)	2(8.0) 23(92.0)	2.917	0.088
ACA n(%)	2(14.3)	3(12.0)	0.042	0.838
MCA n(%)	6(42.9)	8(32.0)	0.460	0.498
PCA n(%)	6(42.9)	14(56.0)	0.620	0.431
AGE Mean(SD)	57.29±12.15	59.80±10.24	-0.688	0.496
NIHSS 0 Mean(SD	23.93±11.91	19.40±7.85	1.432	0.161
Stroke size	10.00(28.00)	8.00(22.40)	0.536	0.595
Stroke volume	28.00(32.00)	20.00(50.00)	0.499	0.621

SIS: Stroke Induced Seizure, NSIS: Non-Stroke Induced Seizures, ACA: Anterior Cerebral Artery, MCA: Middle Cerebral Artery, PCA: Posterior Cerebral Artery, IVH: Intraventricular Haemorrhage, NIHSS: National Institute Health Stroke Scale Score *$p<0.05$ comparing SIS/SIE and NSIS

4.38: Comparison of Socio-biological Characteristics and Mortality Rate among 99 with Non Stroke Induced Seizure and 41 Stroke Induced Epilepsy (14 Seizure only, 14 Seizures to Epilepsy, and 13 Epilepsy only cohorts) treated at Federal Medical Centre, Abeokuta (FMCA) over a period of two years.

Of the 140 participants recruited, 99(70.7%) had NSIS while 41(29.3%) had SIS. Of the 41(29.3%) with SIS, 14(10%) had seizure only, 14(10%) had seizure that progress to epilepsy, and 13(9.3%) had epilepsy only after stroke.

There was a statistically lower mean size [5.00(39.00) vs 12.00(29.00); p≤0.011] and higher ventricular effacement [9(9.1%) vs 5(25.7%); p≤0.015] respectively in the NSIS compared to seizure only group. There was a higher frequency of sleep disorder [2(2.0%) vs 0(0.0%); p≤0.001]. Consistently, MR was higher in the NSIS group compared to seizures only group at 1 month [11(11.1%) vs 5(35.7%); p≤0.023] and 12 months [32(32.3%) vs 9(64.3%); p≤0.016].

Variables n(%)	None N=99	Seizures N=14	Seizures to Epilepsy N=14	Epilepsy N=13	P_1 Value	P_2 Value	P_3 Value
Gender Male Female	 63(63.6) 36(36.4)	 6(42.9) 8(57.1)	 8(57.1) 6(42.9)	 11(84.6) 2(15.40	0.154	0.136	0.133
Stroke type Ischemic Hemorrhagic	 74(74.7) 25(25.3)	 7(50.0) 7(50.0)	 10(71.4) 4(28.6)	 10(76.9) 3(23.1)	0.272	0.054	0.0865
Age (Mean±SD)	61.13±9.85	64.64±13.08	60.43±14.01	67.00±11.21	0.210	0.234	0.049*
NIHSS 0, Mean(SD)	17.95±9.61	24.86±12.93	19.14±9.91	17.00±9.43	0.104	0.018*	0.738
Size, Median(range)	5.00(39.00)	12.00(29.00)	7.00(13.00)	4.00(11.00)	0.011*	0.004*	0.363
Volume in cm^3 Median(range)	10.00(59.0)	30.00(39.00)	20.00(32.50)	18.00(34.50)	0.117	0.025*	0.768
Mass effects	22(22.2)	7(50.0)	3(21.4)	1(7.7)	0.061	0.026*	0.223
Ventricular effacement	9(9.1)	5(25.7)	2(14.3)	0(0.0)	0.015*	0.005*	0.257
Raised ICP	21(21.2)	6(42.9)	4(28.6)	5(38.5)	0.224	0.075	0.166
Hypertension	73(73.7)	11(100.0)	10(71.4)	10(76.9)	0.272	0.052	0.805
Diabetes	16(16.2)	3(27.3)	4(28.6)	3(23.1)	0.576	0.355	0.532
Sleep disorder	2(2.0)	0(0.0)	0(0.0)	3(23.1)	0.001*	0.634	0.001*
1month mortality	11(11.1)	5(35.7)	1(7.1)	0(0.0)	0.023*	0.005*	0.125
3months mortality	27(27.3)	9(64.3)	4(28.6)	1(7.7)	0.010*	0.005*	0.125
6months mortality	30(30.3)	9(64.3)	6(42.9)	1(7.7)	0.012*	0.012*	0.087
12months	32(32.3)	9(64.3)	6(42.9)	1(7.7)	0.016*	0.020*	0.067

mortality							

Table 42: Comparison of Socio-biological Characteristics and Mortality Rate among 99 with Non Stroke Induced Seizure and 41 Stroke Induced Epilepsy (14 Seizure only, 14 Seizures to Epilepsy, and 13 Epilepsy only cohorts) treated at Federal Medical Centre, Abeokuta (FMCA) over a period of two years.

NIHSS: National Institute Health Stroke Scale Score *p<0.05, p1: comparison of none, seizures, seizures to epilepsy and epilepsy, p2: none versus seizures only, p3: none versus epilepsy only.

4.39: Patterns of Mortality among 140 Stroke Patients Treated at Federal Medical Centre, Abeokuta (FMCA) over a period of two years.

Of the 140 participants, 101(72%) had ischaemic stroke while 39(28%) had haemorrhagic stroke. However, out of the 101 ischaemic stroke patients, 63(62.4%) were males and 38(37.6%) were females. Furthermore, of the 39 haemorrhagic stroke patients, 25(64.1%) were males and 14(35.9%) were females. The mortality rate among stroke cohort was 12.1%, 29.3%, 29.3%, 32.9%, 34.3%, and 36.4% at 7 days, 1 month, 3 months, 6 months, 12 months, and 24 months, respectively. Furthermore, of the 39 haemorrhagic stroke patients, 20.5%, 41.0%, 41.0%, 48.7%, 48.7%, and 48.7% died by 7days, 1 month, 3 months, 6 months, 12 months, and 24 months, respectively. On the other hand, 8.9%, 24.8%, 24.8%, 26.1%, 28.7%, and 31.7% died in the ischaemic group. There were higher M:F [60(67.4%) vs 29(32.6%)], lower mean age [59.99±9.80 vs 65.39±11.77; p≤0.004], higher haemorrhagic death

Table 43: Patterns of Mortality among 140 Stroke Patients Treated at Federal Medical Centre, Abeokuta (FMCA) over a period of two years

Variable n(%)	Alive	Dead	Statistics	p value
Gender Male Female	60(67.4) 29(32.60	28(54.9) 23(45.1)	2.175	0.140
Age (Mean±SD)	59.99±9.80	65.39±11.77	-2.915	0.004*
Hypertension	63(73.3)	41(80.4)	0.892	0.345
Diabetics mellitus	16(18.6)	10(19.6)	0.021	0.885
Hyperlipidemia	13(15.1)	9(17.6)	0.152	0.697
Chronic kidney Disease	2(2.3)	1(2.0)	0.020	0.888
Heart Disease	4(4.7)	3(5.9)	0.100	0.752
Stroke Type Ischaemic Haemorrhagic	69(77.5) 20(22.5)	32(62.7) 19(37.3)	3.526	0.060
NIHSS 0, (Mean±SD)	13.57±7.50	27.57±7.61	-10.570	<0.001 *
ACA	14(15.7)	10(19.6)	0.343	0.558
MCA	62(69.7)	25(49.0)	5.873	0.015*
PCA	13(14.6)	17(33.3)	6.753	0.009*
Size, Median(range)	5.00(29.00)	6.00(39.00)	-3.067	0.003*
Mass Effect	10(11.2)	23(45.1)	20.636	0.000*
Small Vessel Disease	12(16.9)	5(15.6)	0.026	0.872
Large Artery	19(26.8)	14(43.8)	2.924	0.087

*p<0.05 comparing dead and alive, SD- Standard Deviation, NIHSS- National Institute of Health Stroke Scale, ACA- Anterior Cerebral Artery, MCA- Middle Cerebral Artery, PCA- Posterior Cerebral Artery, 0: Reading at presentation

Table 44: Predictors of Mortality among 140 Stroke Patients Treated at Federal Medical Centre, Abeokuta (FMCA) over a period of two years

Variables	B	p-value	Odds ratio	95% CI
Age (In Years)	0.035	0.166	1.921	0.986-1.080
NIHSS at presentation	0.219	<0.001*	27.763	1.147-1.350
Stroke Size	0.011	0.797	0.066	0.930-1.100
MCA	-0.824	0.310	1.029	0.089-2.157
PCA	-0.397	0.667	0.185	0.110-4.108
Mass effect	1.632	0.018*	5.578	1.320-19.831

*p<0.05 CI – Confidence Interval B- Beta 0- at presentation MCA – Middle Cerebral Artery PCA – posterior Cerebral Artery NIHSS – National Institute of Health Stroke Scale

4.40: Predictors of SIS/SIE among Ischaemic Stroke Patients Treated at Federal Medical Centre Abeokuta in South Western Nigeria over a period of two year

Use of statin, (Beta coefficient -1.506, p≤0.032, odd ratio 4.588, C.I 0.056-0.888) and cortical involvement (Beta coefficient -1.525, odd ratio 6.044, p≤0.014, C.I 0.064-0.734) were the determinants of SIS among Ischaemic stroke cohorts

Table 45: Predictors of SIS/SIE among Ischaemic Stroke Patients Treated at Federal Medical Centre Abeokuta in South Western Nigeria over a period of two year

Variables	B	p-value	Odds ratio	95% CI
AGE MEAN	-0.039	0.187	1.741	0.907-1.019
Antihypertensive	-1.101	0.152	2.052	0.074-1.500
Statin	-1.506	0.032*	4.588	0.056-0.888
Cortical involvement Cortical Not cortical	-1.525 Reference	0.014*	6.044	0.064-0.734
Raised ICP	-1.354	0.064	3.442	0.062-1.079
PTE	-2.893	0.037	4.349	0.004-0.840
PCA	21.173	0.998	0.000	0.000-

*p<0.05 CI – Confidence Interval B- Beta 0- at presentation

4.41: Predictors of Seizures and Epilepsy among 140 Stroke Patients Treated at Federal Medical Centre Abeokuta in South Western Nigeria over a period of two years

On regression analysis, only sleep disorder (Beta coefficient 2.377, odd ratio 5.437, p≤0.017, C.I 1.542-75.230) predicted SIE. However, nothing predicted SIS.

Table 46: Predictors of Seizures among 140 Stroke Patients Treated at Federal Medical Centre Abeokuta in South Western Nigeria over a period of two years

Variables	B	p-value	Odds ratio	95% CI
NIHSS 0	0.005	0.932	0.007	0903-1.117
Mass effect	-0.157	0.873	0.026	0.124-5.876
Ventricular effacement	0.799	0.455	0.559	0.274-18.077
Stroke size	0.043	0.403	0.698	0.944-1.154
Stroke volume	0.015	0.557	0.344	0.965-1.068
Mortality 30days	-20.539	0.999	0.000	0.000-
Mortality 90days	-1.106	1.000	0.000	0.000-
Mortality 180days	-0.106	1.000	0.000	0.000-
Mortality 360 days	19.549	0.999	0.000	0.000-
Epilepsy				
Age	0.046	0.139	2.194	0.985-1.114
Sleep disorder	2.377	0.017*	5.743	1.542-75.230

*p<0.05 CI – Confidence Interval B- Beta 0- at presentation

4.42: Comparison of EEG Characteristics among 41 Stroke Induced Epilepsy/ Stroke Induced Seizure (22 Carbamazepine versus 19 Levetiracetam) Treated at Federal Medical Centre Abeokuta in South Western Nigeria over period of 2years

The frequency of alpha, theta, and delta were 5(22.7%), 9(40.9%), and 8(36.4%) respectively in the CBZ compare to 4(21.1%), 9(47.4%), 6(31.6%) respectively in LEV group. This is however not statistically significant ($p \leq 0.220$). Similarly, at 12months, the frequency of alpha, theta, delta and intermixed was 7(63.6%), 2(18.2%), 1(9.1%), and 1(9.1%) in the CBZ group compared respectively to 11(73.3%), 2(13.3%), 2(13.3%), 0(0%) and 0(0%) in the LEV group.

4.47: Comparison of EEG Characteristics among 41 Stroke Induced Epilepsy/ Stroke Induced Seizure (22 Carbamazepine versus 19 Levetiracetam) Treated at Federal Medical Centre Abeokuta in South Western Nigeria over period of 2years

Variable	CBZ N (%)	LEV N (%)	p value	Frequency	CBZ N (%)	LEV N (%)	p value
Background at Presentation				Frequency Presentation			
Alpha	5(22.7)	4(21.1)	0.915		6(27.3)	4(21.1)	0.644
Theta	9(40.9)	9(47.4)		Fast	16(72.7)	15(78.9)	
Delta	8(36.4)	6(31.6)		Slow			
Background 6 months				Frequency 6 months			
Alpha	5(38.5)	11(73.3)	0.220				
Theta	5(38.5)	2(13.3)		Fast	5(38.5)	8(53.3)	0.431
Delta	2(15.4)	2(13.3)		Slow	8(61.5)	7(46.7)	
Intermixed slow	1(7.7)	0(0.0)					
Background 12months				Frequency 12months			
Alpha	7(63.6)	11(73.3)	0.649				
Theta	2(18.2)	2(13.3)		Fast	7(63.6)	11(73.3)	0.597
Delta	1(9.1)	2(13.3)		Slow	4(36.4)	4(26.7)	
Intermixed slow	1(9.1)	0(0.0)					
Epileptiform pattern at Presentation				Slowing at Presentation			
Focal	2(9.1)	4(21.1)	0.370				
Generalized	13(59.1)	9(47.4)		Focal	1(4.5)	0(0.0)	0.478
Focal-generalized	2(9.1)	4(21.1)		Generalized	11(50.0)	7(35.8)	
None	5(22.7)	2(10.5)		Intermittent	5(22.7)	8(42.1)	
				None	5(22.7)	4(21.1)	
Epileptiform pattern at 6 months				Slowing at 6 months			
Focal	3(23.1)	4(26.7)	0.530	Focal	-	-	
Generalized	7(53.8)	7(46.7)		Generalized	4(26.7)	3(20.0)	0.890
Focal-generalized	0(0.0)	2(13.3)		Intermittent	5(33.3)	6(40.0)	
None	3(23.1)	2(13.3)		None	6(40.)	6(40.0)	
12month				Slowing at 12months			
Focal	2(18.2)	4(33.3)	0.189				
Generalized	6(54.%	2(16.7)		Focal	-	-	
Focal-generalized	0(0.0)	2(16.7)		Generalized	2(15.4)	3(20.0)	0.928
None	3(27.3)	4(33.3)		Intermittent	5(38.5)	6(40.0)	
				None	6(46.2)	6(40.0)	

CBZ- Carbamazepine LEV – Levetiracetam

4.43 Socio-biological Characteristics of 41 Patients Treated with Levetiracetam or Carbamazepine at Federal Medical Centre Abeokuta in South Western Nigeria over a period of one year

Of the 41 participants that developed SIS/SIE, 25(61%) were males and 16(39%) were females ($p<0.001$). The socio-demographic, clinical characteristics, and MR of participant with seizures only that are on CBZ were statistically comparable to those on LEV except for MR at 12months ($p\leq0.028$), CSID at 12months ($p\leq0.045$), CSID at 24months ($p\leq0.012$) and MR at 24month ($p\leq0.014$).

4.48 Socio-biological Characteristics of 92 Patients Treated with Levetiracetam or Carbamazepine at Federal Medical Centre Abeokuta in South Western Nigeria over a period of one year

Variables	CBZ n=22	LEV n=19	p value
Gender Male N(%) Female N(%)	 8(36.4) 14(63.6)	 17(89.5) 2(10.5)	 0.001*
NIHSS at 1month Not severe Severe	 7(31.8) 15(68.2)	 6(42.9) 8(57.1)	 0.385
NIHSS at 1year Not severe Severe	 8(36.3) 14(63.7)	 8(57.2) 6(42.9)	 0.591
MRS at 1 month Good outcome N(%) Poor outcome N(%)	 5(22.7) 17(77.3)	 9(47.4) 10(52.6)	 0.097
MRS at 1 year Good outcome N(%) Poor outcome N(%)	 7(31.8) 15(68.2)	 11(57.9) 8(42.1)	 0.093
Mortality at 1 month N(%)	10(45.5)	4(21.1)	0.100
Mortality at 1 year N(%)	12(54.5)	4(21.1)	0.028*
CSID AT 1month CI n(%) NCI n(%)	 19(86.4) 3(13.6)	 13(68.4) 6(31.6)	 0.166
CSID at 1year CI n(%) NCI n(%)	 5(50.0) 5(50.0)	 2(13.3) 13(86.7)	 0.045*

*p<0.05 comparing CBZ and LEV CBZ- Carbamazepine LEV – Levetiracetam CI – Cognitively Impaired NCI – Non Cognitively Impaired

4.49 Socio-biological Characteristics of 92 Patients Treated with Levetiracetam or Carbamazepine at Federal Medical Centre Abeokuta in South Western Nigeria over a period of one year

Variables	CBZ	LEV	p value
NIHSS at 2years Not severe Severe	 7(31.8) 15(69.2)	 4(40.0) 6(60.0)	0.434
MRS at 2 years Good outcome N(%) Poor outcome N(%)	 6(27.3) 16(72.7)	 9(60.0) 6(40.0)	0.047
Mortality at 2 years N(%)	13(59.1)	4(21.1)	0.014*
CSID at 2years CI NCI	 5(55.6) 4(44.4)	 0(0.0) 8(100.0)	0.012*

*p<0.05 comparing CBZ and LEV CBZ- Carbamazepine LEV – Levetiracetam CI – Cognitively Impaired NCI – Non Cognitively Impaired

Olabisi Onabanjo University Teaching Hospital Sagamu

4.44: Socio-biological Characteristics of 121 Stroke Patients with Stroke Induced Seizure and Stroke Induced Epilepsy Treated at Olabisi Onabanjo University Teaching Hospital (OOUTH) over a period of two years

Of the 121 stroke patients recruited from FMCA, 72(59.5%) were males while 49(40.5%) were females. A total of 91(75%) had ischaemic stroke while 30(25%) had haemorrhagic stroke. A total of 21(17%) developed seizure disorder following stroke. Of the 91 participants with ischaemic stroke, 14(15%) developed seizures whereas seizure was recorded among 7 of the 30 individuals who had haemorrhagic stroke, (15% vs 23%).

Furthermore, 100(82.6%) of the participants had no seizure, of the 21 patients that developed seizure 2(1.7%), 13(10.7%), and 6(5.0%) had seizures only, seizure to epilepsy and epilepsy only respectively.

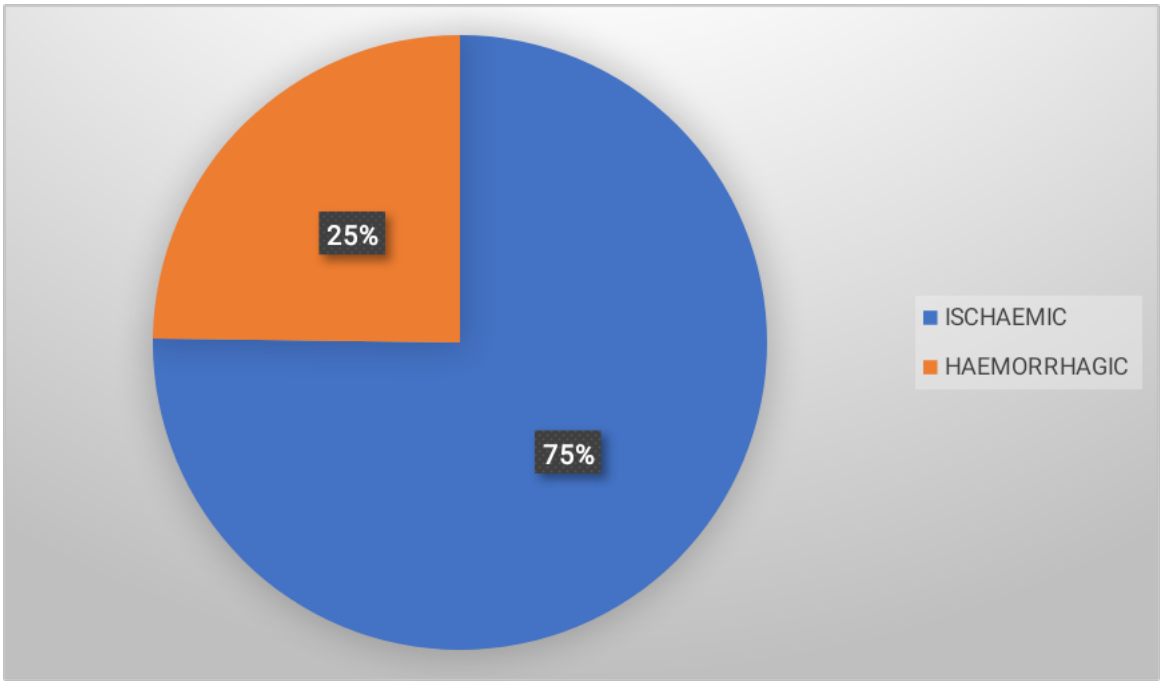


Figure 4.20: Stroke classification based on type among 346 cohorts Treated at Olabisi Onabanjo University Teaching Hospital in South Western Nigeria for a period of two years

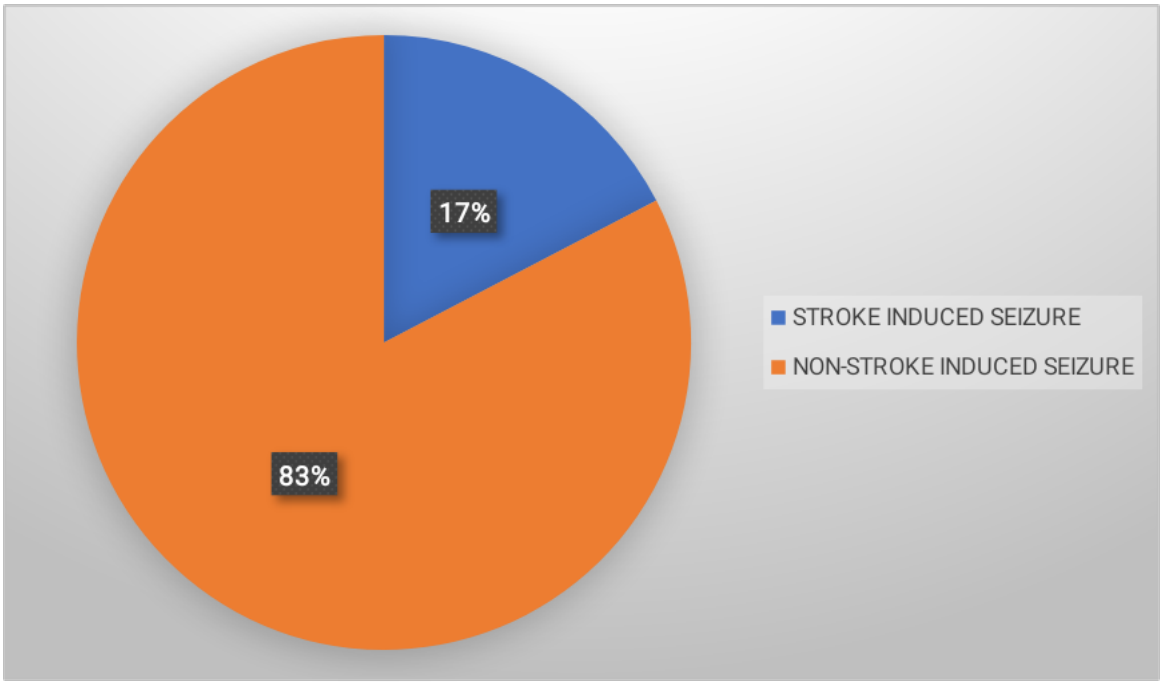


Figure 4.21: Stroke classification based on Seizure Occurrence/presence of Seizure among 92 Post-Stroke Seizure and 254 NSIS Patients Treated at Olabisi Onabanjo University Teaching Hospital in South Western Nigeria for a period of two years

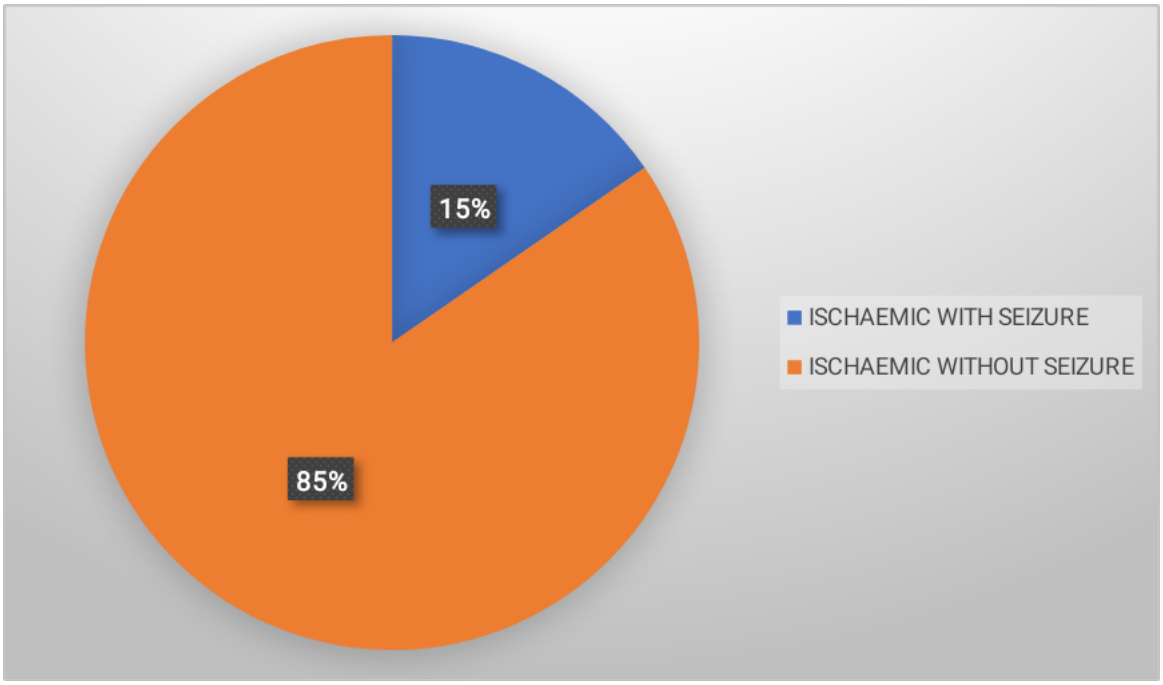


Figure 4.22: The Frequency of Haemorrhagic Stroke Participants with Stroke Induced Seizure and Non-Stroke Induced Seizure Treated at Olabisi Onabanjo University Teaching Hospital in South Western Nigeria for a period of two years

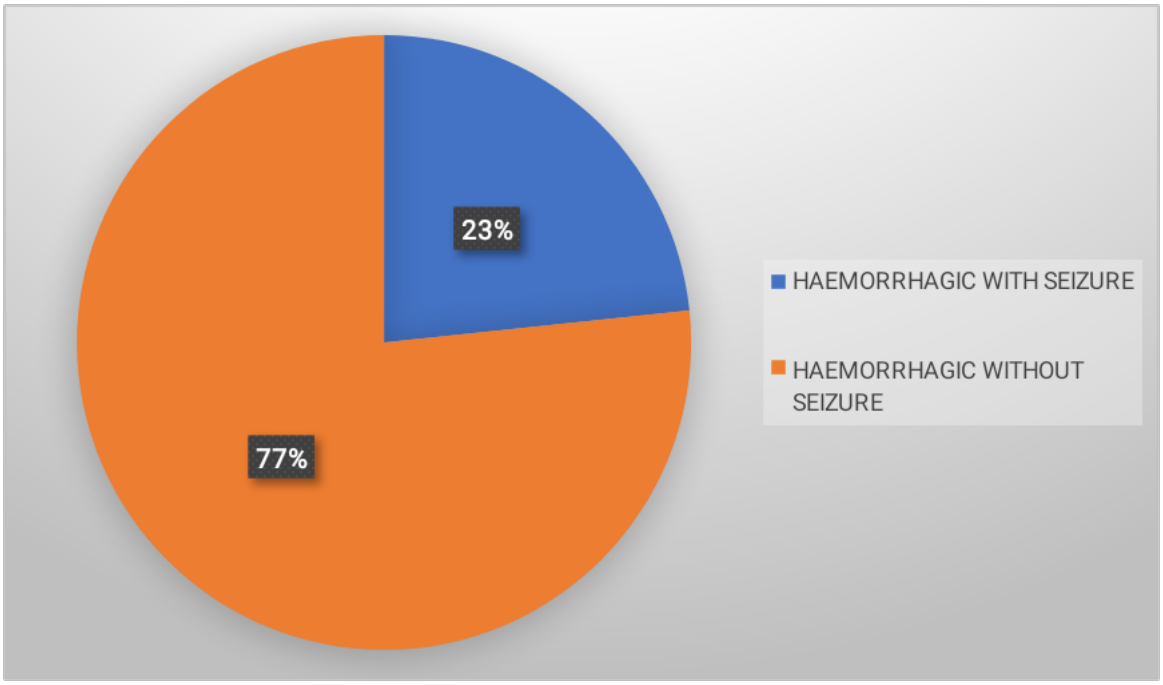


Figure 4.23: The Frequency of Ischaemic Stroke Participants with Stroke Induced Seizure and Non-Stroke Induced Seizure Treated at Olabisi Onabanjo University Teaching Hospital in South Western Nigeria for a period of two years

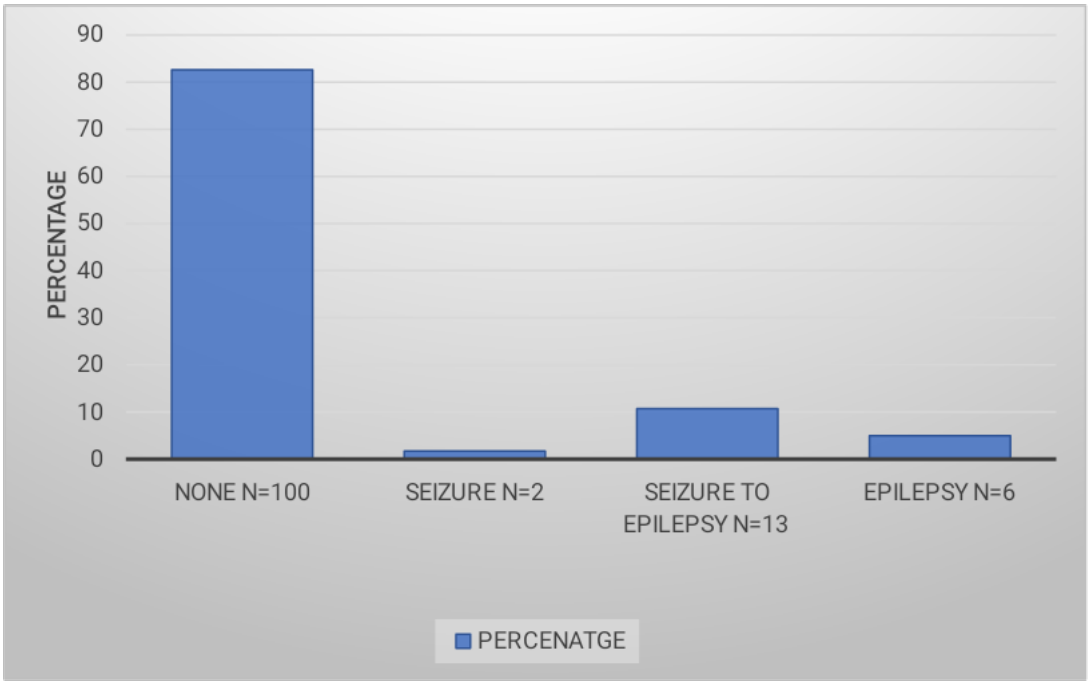


Figure 4.24: Frequency of Seizure and Epilepsy among Stroke Patients Treated at Olabisi Onabanjo University Teaching Hospital in South Western Nigeria for a period of two years.

4.45 Comparison of Clinical characteristics of Stroke Survivors with or without Seizure treated at Olabisi Onabanjo University Teaching Hospital (OOUTH) over a period of two years.

Patterns of stroke location revealed that there were higher number of participants with ischaemic stroke at frontal lobe [36(39.6%) vs 0(0.0%); p <0.001], parietal lobe [41(45.1%) vs 6(20.0%); p ≤0.015], and lower number of participants at occipital lobe [5(5.5%) vs 6(20.0%); p ≤0.017], caudate [0(0.0%) vs 2(6.7%); p ≤0.013], lentiform [6(6.6%) vs 10(33.3%); p <0.001] and thalamus [6(6.6%) vs 12(40.0%); p <0.001] respectively compared to haemorrhagic stroke.

Among participants with ACA, 27(29.7%) were ischemic while 3(10.0%) were haemorrhagic stroke (p ≤0.030). In the PCA region, 12(13.2%) were ischaemic while 11(36.7%) were haemorrhagic (p≤0.004).

The use of statin was seen among 33(26.3%) ischemic stroke cohort and 3(10.0%) among haemorrhagic stroke cohort and this was statistically significant (p ≤0.006). The median stroke size was 3.00(39.00) among ischaemic stroke cohort and 10.00(37.00) among haemorrhagic stroke cohort which is statistically significant (p <0.001).

Table 50: Comparison of Clinical characteristics of Stroke Survivors with or without Seizure treated at Olabisi Onabanjo University Teaching Hospital (OOUTH) over a period of two years.

Variables	Ischaemic n= 91	Haemorrhagic n = 30	Total N=121	x^2 Value	p Value
A. Clinical Characteristics					
Gender n (%) Male Female	 53(58.2) 38(41.8)	 19(63.3) 11(36.7)	 72(59.5) 49(40.50	0.243	0.622
NIHSS at Presentation Mean±SD	14.74±8.21	17.00±9.37		-1.263	0.209
Stroke Severity n (%) No stroke Minor stroke Moderate stroke Moderate to severe Severe stroke	 2(2.2) 8(8.8) 41(45.1) 20(22.0) 20(22.0)	 1(3.3) 1(3.3) 14(46.7) 2(6.7) 12(40.0)	 3(2.5) 9(7.4) 55(45.5) 22(18.2) 32(26.4)	6.714	0.152
Stroke size median (range)	3.00(39.00)	10.00(37.00)		-5.152	<0.001 *
Hypertensive n(%) Anti-hypertensive n(%)	56(61.5) 43(47.3)	16(53.3) 11(36.7)	72(59.5) 54(22.6)	0.630 1.023	0.427 0.312
Diabetics n(%) Anti-diabetics n(%)	18(19.8) 9(10.0)	2(6.7) 1(3.3)	20(16.5) 10(8.3)	2.812 1.309	0.094 0.253
Statin n(%)	33(26.3)	3(10.0)	36(29.8)	7.446	0.006*
Mass effect n(%)	6(6.6)	21(70.0)	27(22.3)	52.327	<0.001 *
Raised ICP n(%)	13(14.3)	9(30.0)	22(18.2)	3.745	0.053
Aspiration pneumonia n(%)	6(6.6)	4(13,3)	10(8.3)	1.352	0.245

PTE n(%)	1(1.1)	1(3.3)	2(1.7)	0.693	0.405
B. Location					
Basal ganglia n(%) Caudate Lentiform	 0(0.0) 6(6.6)	 2(6.7) 10(33.3)	 2(1.7) 16(13.2)	 6.169 14.059	 0.013* <0.001 *
Lobar Involvement n(%) Frontal Lobe Parietal Lobe Temporal Lobe Occipital Lobe	 3639.6) 41(45.1) 12(13.2) 5(5.5)	 0(0.0) 6(20.0) 2(6.7) 6(20.0)	 36(29.8) 47(38.8) 14(11.6) 11(9.1)	 16.895 5.962 0.937 5.744	 <0.001 * 0.015* 0.333 0.017*
Subcortical n(%) Internal Capsule Thalamus	 5(5.6) 6(6.6)	 3(10.0) 12(40.0)	 8(6.6) 18(14.9)	 0.742 19.884	 0.389 <0.001 *
Infratentorial n(%) Cerebellum Brain stem Pons Midbrain	 5(5.7) 3(3.3) 1(1.1)	 0(0.0) 0(0.0) 0(0.0)	 5(4.2) 3(2.5) 1(0.8)	 1.780 1.014 0.332	 0.182 0.314 0.564
Cortical Involvement n(%) Cortical No cortical	 15(16.5) 76(83.5)	 5(16.7) 25(83.3)	 20(16.5) 101(83.5)	 0.001	 0.981
Age grouped <35 36-70 71-95	 5(5.5) 67(73.6) 19(20.9)	 0(0.0) 29(96.7) 1(3.3)	 5(4.1) 96(79.3) 20(16.5)	 7.360	 0.025*
C. Arterial Territory					
ACA n(%) MCA n(%)	27(29.7) 53(58.2)	3(10.0) 16(53.3)	30(24.8) 69(57.0)	4.682 0.222	0.030* 0.638

PCA n(%)	12(13.2)	11(36.7)	23(19.0)	8.080	0.004*

NIHSS – National Institute of Health Stroke Scale Score PTE: Pulmonary Thromboembolism, ICP: Intracranial Pressure, ACA: Anterior Cerebral Artery, MCA: Middle Cerebral Artery, PCA: Posterior Cerebral Artery, *p<0.05 comparing ischaemic and haemorrhagic

4.46 Mortality Rate among 121 Participants Treated at Olabisi Onabanjo University Teaching Hospital (OOUTH) for a period of two years.

The mortality rate among stroke cohort was 1.7%, 5.0%, 16.5%, 22.3%, 22.3%, and 28.1% at 7 days, 1 month, 3 months, 6 months, 12 months, and 24 months, respectively. Furthermore, mortality rate was higher among haemorrhagic stroke cohort compared to ischemic stroke cohort from 7 days to 24 months and these were consistently statistically significant.

4.51 Mortality Rate among 121 Participants Treated at Olabisi Onabanjo University Teaching Hospital (OOUTH) for a period of two years.

Variables	7days	1months	3months	6months	12months	24months
Stroke Patient n(%)	2(1.7)	6(5.0)	20(16.5)	27(22.3)	27(22.3)	34(28.1)
Ischaemic n(%)	1(1.1)	3(3.3)	11(12.1)	17(18.7)	17(18.7)	24(26.4)
Haemorrhagic n(%)	1(3.3)	3(10.0)	9(30.0)	10(33.3)	10(33.3)	10(33.3)
SIS n(%)	-	2(9.5)	3(14.3)	3(14.3)	3(14.3)	5(23.8)
Seizure type						
ISPWS n(%)	-	1(7.1)	1(7.1)	1(7.1)	1(7.1)	3(21.4)
HSPWS n(%)	-	1(14.3)	2(28.6)	2(28.6)	2(28.6)	2(28.6)

SIS – Stroke Induced Seizures ISCH- Ischaemic Stroke Patients with Seizures HSPWS Haemorrhagic Stroke Patients with Seizures

4.47: Comparison of Sociodemographic Clinical Characteristics among 91 Ischemic Stroke Patients and 30 Haemorrhagic Stroke Patients with Stroke Induced Epilepsy

Among 21 patients that developed SIE, 12(57.1%) were males and 9(42.9%) were females. There were 14(66.7%) ischemic and 7(33.3%) haemorrhagic stroke participants that developed SIE. The mean age of participants with SIE among ischaemic stroke patients is 2.14±0.54 compared to a value of 2.14±0.38 among haemorrhagic stroke patient with SIE. The mean stroke volume among participants with ischaemic stroke with SIE is 2.70(39.00) compared to the value of 30.00(25.00) among those with haemorrhagic stroke with SIE and this was significant ($p<0.001$).

Among the 21 patients with SIE, the frequency of antihypertensive usage was 7(50.0%) among ischemic cohorts compared to 0(0.0%) among haemorrhagic stroke patients and this was significant ($p\leq0.022$). Also, the frequency of statin usage was 6(42.9%) among ischaemic cohorts compared to 0(0.0%) among haemorrhagic stroke patients ($p\leq0.040$).

Furthermore, the presence of mass effect was more among haemorrhagic cohorts 4(57.1%) compared to 0(0.0%) among ischemic cohorts ($p\leq0.002$).

Table 62: Comparison of Sociodemographic Clinical Characteristics among 91 Ischemic Stroke Patients and 30 Haemorrhagic Stroke Patients with Stroke Induced Epilepsy

Variables	ISPWS n=14	HMPWS n=7	x^2 value	p value
Gender n(%) Male Female	 6(42.9) 8(57.1)	 6(85.7) 1(14.3)	 3.500	 0.061
Age Mean (SD)	2.14±0.54	2.14±0.38	0.000	1.000
Stroke size Median (Range)	1.60(29.00)	12.00(9.00)	3.496	0.077
Stroke volume cm^3 Median (Range)	2.70(39.00)	30.00(25.00)	23.990	<0.001*
Cortical involvement n(%) Cortical No cortical	 3(21.4) 11(78.6)	 4(57.1) 3(42.9)	 2.679	 0.102
Hypertensive n(%)	8(57.1)	0(0.0)	6.462	0.011*
Diabetics n(%)	5(35.7)	0(0.0)	3.281	0.070
ACA n(%)	4(28.6)	2(28.60	0.000	1.000
MCA n(%)	9(64.3)	4(57.1)	0.101	0.751
PCA n(%)	1(7.1)	1(14.3)	0.276	0.599
Antihypertensive n(%)	7(50.0)	0(0.0)	5.250	0.022*
Anti-diabetics n(%)	4(28.6)	0(0.0)	2.471	0.116
Statin n(%)	6(42.9)	0(0.0)	4.200	0.040*
Mass effect n(%)	0(0.0)	4(57.1)	9.882	0.002*

ACA: Anterior Cerebral Artery, MCA: Middle Cerebral Artery, PCA: Posterior Cerebral Artery, PTE: Pulmonary Thromboembolism, UTI: Urinary Tract Infection, ICP: Intracranial Pressure, ISPWS: Ischaemic Stroke Patients with Seizures, HSPWS: Haemorrhagic Stroke Patients with Seizures, *p<0.05 comparing ISPWS and HMPWS

4.48 Comparison of Socio-biological Characteristics between Participants with Ischemic Stroke with or without seizure treated at Olabisi Onabanjo University Teaching Hospital (OOUTH) over a period of two years.

Of the 91(75%) participants with ischemic stroke, 14(15.4%) had SIS/SIE with 6(42.9%) males and 8(57.1%) females. Concerning use of anti-diabetics, 4(28.6%) of ischemic SIS/SIE used anti-diabetics while 27(35.1%) of ischemic NSIS used anti-diabetics ($p \leq 0.012$). Furthermore, 12(85.7%) among ischemic cohorts with SIS/SIE had theta background frequency compared to 34(44.2%) among NSIS which was significant ($p \leq 0.014$). There was a significant difference between ischemic cohort with SIS/SIE and NSIS with regards to sleep disorder ($p \leq 0.018$).

Table 63: Comparison of Socio-biological Characteristics between Participants with Ischemic Stroke with or without seizure treated at Olabisi Onabanjo University Teaching Hospital (OOUTH) over a period of two years

Variable n(%)	SIS/SIE n=14	NSIS n=77	Statistics	p-value
Gender Male Female	 6(42.9) 8(57.1)	 47(61.0) 30(39.0)	1.610	0.204
Mass effect	0(0.0)	6(7.8)	1.168	0.280
Antihypertensive	7(50.0)	36(46.8)	0.050	0.823
Anti-diabetics	4(28.6)	5(6.6)	6.353	0.012*
Statin	6(42.9)	27(35.1)	0.311	0.577
Raised ICP	2(14.3)	11(14.3)	0.000	1.000
Aspiration pneumonia	0(0.0)	6(7.8)	1.168	0.280
PTE	0(0.0)	1(1.3)	0.184	0.668
UTI	0(0.0)	8(10.4)	1.595	0.207
Hypertension	8(57.1)	48(62.3)	0.135	0.713
Diabetes mellitus	5(35.7)	13(16.9)	2.647	0.104
Sleep disorder	1(7.1)	0(0.0)	5.561	0.018*
Cortical involvement Cortical Not cortical	 3(21.4) 11(78.6)	 12(15.6) 65(84.4)	0.294	0.588
ACA n(%)	4(28.6)	23(29.9)	0.010	0.922
MCA n(%)	9(64.3)	44(57.1)	0.249	0.618
PCA n(%)	1(7.1)	11(14.3)	0.528	0.467
AGE Mean(SD)	57.00(14.98	59.13(13.31	-0.540	0.590

NIHSS 0 Mean(SD	15.21(10.09	14.65(7.90	0.235	0.814
Stroke size	1.60(29.00)	3.00(39.00)	0.164	0.870
Stroke volume	2.75(39.5)	5.00(54.00)	-0.470	0.685

SIS: Stroke Induced Seizure Patients, NSIS: Non-Stroke Induced Seizures, ACA: Anterior Cerebral Artery, MCA: Middle Cerebral Artery, PCA: Posterior Cerebral Artery, IVH: Intraventricular Haemorrhage, NIHSS: National Institute Health Stroke Scale Score *p<0.05 comparing SIS/SIE and NSIS

Table 64: Comparison of Socio-biological Characteristics between Participants with Ischemic Stroke with or without seizure treated at Olabisi Onabanjo University Teaching Hospital (OOUTH) over a period of two years

Variable n(%)	SIS/SIE n=14	NSIS n=77	Statistics	p-value
Background Alpha Theta Delta Intermixed fast	 0(0.0) 12(85.7) 2(14.3) 0(0.0)	 34(44.2) 34(44.2) 8(10.4) 1(1.3)	10.575	0.014*
Epileptiform Focal Generalized Focal - generalized No	 1(7.1) 2(14.3) 8(57.1) 3(21.4)	 1(1.3) 13(16.9) 23(29.9) 40(51.9)	6.811	0.078

SIS: Stroke Induced Seizure Patients, NSIS: Non-Stroke Induced Seizures, *p<0.05 comparing SIS/SIE and NSIS

4.49: Comparison of Socio-biological Characteristics between participants with Haemorrhagic Stroke with or without Seizure treated at Olabisi Onabanjo University Teaching Hospital (OOUTH) over the period of two years.

Of the 30 participants with haemorrhagic stroke, 7(23.3%) had SIS/SIE while 23(76.7%) had NSIS. Of the 7 haemorrhagic cohort with SIS/SIE, 6(85.7%) were males compared to 1(14.3%) females while haemorrhagic cohort with NSIS comprised 13(56.5%) males and 10(43.5%) females. Furthermore, 0(0.0%) of individuals with haemorrhagic SIS/SIE had background hypertension whereas 16(69.6%) of hemorrhagic NSIS had hypertension. Concerning use of antihypertensive, 0(0.0%) of haemorrhagic SIS/SIE used antihypertensive while 11(47.8%) of haemorrhagic NSIS used antihypertensive ($p \leq 0.021$). Again, presence of cortical involvement of cranial CT was higher 4(57.1%) in haemorrhagic stroke patient with SIS/SIE compared to 1(4.3%) NSIE ($p \leq 0.001$).

Furthermore, there was a significant difference between haemorrhagic cohort with SIS/SIE and NSIS with regards to raised ICP ($p \leq 0.048$).

Table 65: Comparison of Socio-biological Characteristics between participants with Haemorrhagic Stroke with or without Seizure treated at Olabisi Onabanjo University Teaching Hospital (OOUTH) over the period of two years.

Variable n(%)	SIS/SIE n=7	NSIS n=23	Statistics	p-value
Gender Male Female	6(85.7) 1(14.3)	13(56.5) 10(43.5)	1.969	0.161
Mass effect	4(57.1)	17(73.9)	0.719	0.397
Antihypertensive	0(0.0)	11(47.8)	5.286	0.021*
Anti-diabetics	0(0.0)	1(4.3)	0.315	0.575
Statin	0(0.0)	3(13.0)	1.014	0.314
Raised ICP	0(0.0)	9(39.1)	3.913	0.048*
Aspiration pneumonia	2(28.6)	2(8.7)	1.835	0.176
IVH	6(85.7)	13(56.5)	1.969	0.161
Hypertension	0(0.0)	16(69.6)	10.435	0.001*
Diabetes mellitus	0(0.0)	2(8.7)	0.652	0.419
Cortical involvement Cortical Not cortical	4(57.1) 3(42.9)	1(4.3) 22(95.7)	10.770	0.001*
ACA n(%)	2(28.6)	1(4.3)	3.499	0.061
MCA n(%)	4(57.1)	12(52.2)	0.053	0.818
PCA n(%)	1(14.3)	10(43.50	1.969	0.161
AGE Mean(SD)	52.57±9.61	55.57±8.34	-0.804	0.429
NIHSS 0 Mean(SD	12.86±7.71	18.26±9.62	-1.355	0.186
Stroke size	12.00(9.00)	8.00(37.00)	-0.458	0.651
Stroke volume	30.00(25.00)	24.00(36.0	-0.563	1.000

		0)		

SIS: Stroke Induced Seizure, NSIS: Non-Stroke Induced Seizures, ACA: Anterior Cerebral Artery, MCA: Middle Cerebral Artery, PCA: Posterior Cerebral Artery, IVH: Intraventricular Haemorrhage, NIHSS: National Institute Health Stroke Scale Score *p<0.05 comparing SIS/SIE and NSIS

Table 66: Comparison of Socio-biological Characteristics between participants with Haemorrhagic Stroke with or without Seizure treated at Olabisi Onabanjo University Teaching Hospital (OOUTH) over the period of two years.

Variable n(%)	SIS/SIE n=14	NSIS n=25	Statistics	p-value
Background Alpha Theta Delta	 0(0.0) 4(57.1) 3(42.9)	 4(17.4) 12(52.2) 7(30.4)	1.491	0.475
Slowing Generalized Intermittent No	 4(57.1) 1(14.3) 2(28.60	 6(26.1) 11(47.8) 6(26.1)	3.075	0.215

SIS: Stroke Induced Seizure, NSIS: Non-Stroke Induced Seizures, ACA: Anterior Cerebral Artery, MCA: Middle Cerebral Artery, PCA: Posterior Cerebral Artery, IVH: Intraventricular Haemorrhage, NIHSS: National Institute Health Stroke Scale Score *p<0.05 comparing SIS/SIE and NSIS

4.50: Comparison of Socio-biological Characteristics and Mortality Rate among 100 with Non Stroke Induced Seizure and 21 Stroke Induced Epilepsy (2 Seizure only, 13 Seizures to Epilepsy, and 6 Epilepsy only cohorts) treated at Olabisi Onabanjo University Teaching Hospital (OOUTH) over a period of two years.

Of the 121 participants recruited, 100(82.6%) had NSIS while 21(17.4%) had SIS. Of the 21(17.4%) with SIS, 2(1.7%) had seizure only, 13(10/7%) had seizure that progress to epilepsy, and 6(5.0%) had epilepsy only after stroke.

There was a statistically lower mean size [5.00(39.00) vs 12.00(29.00); p≤0.011] and higher ventricular effacement [9(9.1%) vs 5(25.7%); p≤0.015] respectively in the NSIS compared to seizure only group. There was a higher frequency of sleep disorder [2(2.0%) vs 0(0.0%); p≤0.001]. Consistently, MR was higher in the NSIS group compared to seizures only group at 1 month [11(11.1%) vs 5(35.7%); p≤0.023] and 12 months [32(32.3%) vs 9(64.3%); p≤0.016].

Table 67: Comparison of Socio-biological Characteristics and Mortality Rate among 100 with Non Stroke Induced Seizure and 21 Stroke Induced Epilepsy (2 Seizure only, 13 Seizures to Epilepsy, and 6 Epilepsy only cohorts) treated at Olabisi Onabanjo University Teaching Hospital (OOUTH) over a period of two years

Variables n(%)	None N=99	Seizures N=14	Seizures to Epilepsy N=14	Epilepsy N=13	P_1 Value	P_2 Value	P_3 Value
Gender Male Female	 60(60.0) 40(40.0)	 1(50.0) 1(50.0)	 7(53.8) 6(46.2)	 4(66.7) 2(33.3)	0.943	0.775	0.746
Stroke type Ischaemic Haemorrhagic	 77(77.0) 23(23.0)	 2(100.0) 0(0.0)	 8(61.5) 5(38.5)	 4(66.7) 2(33.3)	0.499	0.441	0.563
Age (Mean±SD)	58.31±12.40	53.00±11.31	58.00±12.44	51.00±16.49	0.533	0.697	0.117
NIHSS 0, Mean(SD)	15.48±8.41	27.00±15.56	13.38±8.09	12.50±8.09	0.164	0.061	0.401
Size, Median(range)	4.00(39.00)	16.50(27.00)	6.00(14.00)	1.10(5.00)	0.146	0.071	0.231
Volume in cm^3 Median(range)	9.00(54.00)	25.00(30.00)	13.00(44.00)	1.50(19.50)	0.175	0.205	0.290
Mass effects	23(23.0)	0(0.0)	4(30.8)	0(0.0)	0.414	0.441	0.184
Ventricular effacement	10(10.0)	0(0.0)	0(0.0)	0(0.0)	0.515	0.638	0.416
Raised ICP	20(20.0)	0(0.0)	2(15.4)	0(0.0)	0.558	0.481	0.224
Hypertension	64(64.0)	2(100.0)	5(38.5)	1(16.7)	0.027*	0.291	0.021*
Diabetes	15(15.0)	2(100.0)	3(23.1)	0(0.0)	0.008*	0.001*	0.306
Sleep disorder	1(1.0)	0(0.0)	3(23.1)	0(0.0)	0.000*	0.887	0.806
1month mortality	4(4.0)	1((50.0)	1(7.7)	0(0.0)	0.025*	0.003*	0.617
3months	17(17.)	1(50.0)	2(15.4)	0(0.0)	0.417	0.225	0.270

mortality							
6months mortality	24(24.0)	1(50.0)	2(15.4)	0(0.0)	0.372	0.397	0.172
12months mortality	24(24.0)	1(50.0)	2(15.4)	0(0.0)	0.372	0.397	0.172

NIHSS: National Institute Health Stroke Scale Score *p<0.05, p1: comparison of none, seizures, seizures to epilepsy and epilepsy, p2: none versus seizures only, p3: none versus epilepsy only

4.51: Patterns of Mortality among 140 Stroke Patients Treated at Olabisi Onabanjo University Teaching Hospital (OOUTH) over a period of two years.

Of the 140 participants, 101(72%) had ischaemic stroke while 39(28%) had haemorrhagic stroke. However, out of the 101 ischaemic stroke patients, 63(62.4%) were males and 38(37.6%) were females. Furthermore, of the 39 haemorrhagic stroke patients, 25(64.1%) were males and 14(35.9%) were females. The mortality rate among stroke cohort was 12.1%, 29.3%, 29.3%, 32.9%, 34.3%, and 36.4% at 7 days, 1 month, 3 months, 6 months, 12 months, and 24 months, respectively. Furthermore, of the 39 haemorrhagic stroke patients, 20.5%, 41.0%, 41.0%, 48.7%, 48.7%, and 48.7% died by 7days, 1 month, 3 months, 6 months, 12 months, and 24 months, respectively. On the other hand, 8.9%, 24.8%, 24.8%, 26.1%, 28.7%, and 31.7% died in the ischemic group. There were higher M:F [60(67.4%) vs 29(32.6%)], lower mean age [59.99±9.80 vs 65.39±11.77; p≤0.004], higher haemorrhagic death

Table 68: Patterns of Mortality among 140 Stroke Patients Treated at Olabisi Onabanjo University Teaching Hospital (OOUTH) over a period of two years

Variable n(%)	Alive	Dead	Statistics	p value
Gender Male Female	51(58.6) 36(41.4)	21(61.8) 13(38.2)	0.100	0.751
Age (Mean±SD)	2.06±0.41	2.29±0.46	-2.735	0.007*
Hypertension	51(58.6)	21(61.8)	0.100	0.751
Diabetics mellitus	16(18.4)	4(11.8)	0.778	0.378
Hyperlipidemia	14916.1)	8(23.5)	0.909	0.340
Chronic kidney Disease	1(1.1)	0(0.0)	0.394	0.530
Heart Disease	5(5.70	3(8.8)	0.375	0.540
Stroke Type Ischaemic Haemorrhagic	67(77.0) 20(23.0)	24(70.6) 10(29.4)	0.541	0.462
NIHSS 0, (Mean±SD)	12.83±6.86	21.62±9.21	-5.730	<0.001*
ACA	22(25.3)	8(23.5)	0.041	0.840
MCA	49(56.3)	20(58.8)	0.062	0.803
PCA	17(19.5)	6(17.6)	0.057	0.811
Size, Median(range)	3.00(39.00)	4.50(39.00)	-2.693	0.008*
Mass Effect	17(19.5)	10(29.4)	1.374	0.241
Small Vessel Disease	13(19.4)	3(12.5)	0.581	0.446
Large Artery	17(25.4)	10(41.7)	2.248	0.134

*p<0.05 comparing dead and alive, SD- Standard Deviation, NIHSS- National Institute of Health Stroke Scale, ACA- Anterior Cerebral Artery, MCA- Middle Cerebral Artery, PCA- Posterior Cerebral Artery, 0: Reading at presentation

Table 69: Predictors of Mortality among 140 Stroke Patients Treated at Olabisi Onabanjo University Teaching Hospital (OOUTH) over a period of two years

Variables	B	p-value	Odds ratio	95% CI
Age (In Years)	0.017	0.388	0.745	0.978-1.058
NIHSS 0	0.134	<0.001*	17.084	1.073-1.218
Stroke Size	0.062	0.062	3.481	0.997-1.135

*p<0.05 NIHSS- National Institute of Health Stroke Scale, 0: Reading at presentation

Table 70: Predictors of SIS/SIE among Ischaemic Stroke Patients Treated at Olabisi Onabanjo University Teaching Hospital in South Western Nigeria over a period of two year

Variables A	B	p-value	Odds ratio	95% CI
Antidiabetics	-2.516	0.039*	4.251	0.007-0.883
Sleep disorder	-20.104	1.000	0.000	0.000-
Background 0 Alpha Theta Delta Intermixed fast	 0.752 -19.786 -19.817 Reference	 1.000 1.000 1.000	 0.000 0.000 0.000	 0.000- 0.000- 0.000-
B				
Antihypertensive	-18.604	0.999	0.000	0.000-
Hypertension	39.359	0.998	0.000	0.000-
Raised ICP	20.049	0.999	0.000	0.000-
Cortical involvement Cortical Not cortical	 -20.219 Reference	 0.999	 0.000	 0.000-

A – Ischaemic B – Haemorrhagic

4.52: Predictors of Seizures and Epilepsy among 140 Stroke Patients Treated at Three Selected Hospitals in South Western Nigeria over a period of two years

On regression analysis, there was no predictors for SIS and SIE.

Table 71: Predictors of Seizures and Epilepsy among 140 Stroke Patients Treated at Three Selected Hospitals in South Western Nigeria over a period of two years

Variables	B	p-value	Olds ratio	95% CI
A				
Diabetes mellitus	-34.184	0.995	0.000	0.000-
Mortality 30days	19.160	0.996	0.000	0.000-
B				
Hypertension	2.185	0.050	9.380	0.999-79.069

A – Seizure B – Epilepsy CI – Confidence Interval

4.52: Comparison of EEG Characteristics among 41 Stroke Induced Epilepsy/ Stroke Induced Seizure (22 Carbamazepine versus 19 Levetiracetam) Treated at Federal Medical Centre Abeokuta in South Western Nigeria over period of 2years

The frequency of alpha, theta, and delta were 5(22.7%), 9(40.9%), and 8(36.4%) respectively in the CBZ compare to 4(21.1%), 9(47.4%), 6(31.6%) respectively in LEV group. This is however not statistically significant ($p \leq 0.220$). Similarly, at 12months, the frequency of alpha, theta, delta and intermixed was 7(63.6%), 2(18.2%), 1(9.1%), and 1(9.1%) in the CBZ group compared respectively to 11(73.3%), 2(13.3%), 2(13.3%), 0(0%) and 0(0%) in the LEV group.

Table 72: Comparison of EEG Characteristics among 21 Stroke Induced Epilepsy/ Stroke Induced Seizure (13 Carbamazepine versus 8 Levetiracetam) Treated at Federal Medical Centre Abeokuta in South Western Nigeria over period of 2years

Variable	CBZ N (%)	LEV N (%)	p value	Frequency	CBZ N (%)	LEV N (%)	p value
Background at Presentation Theta Delta	8(61.5) 5(38.5)	8(100.0) 0(0.0)	0.044*	Frequency Presentation Fast Slow	13(100.0)	8(100.0)	
Background 6 months Alpha Theta Delta	5(50.) 3(30.0) 2(20.0)	6(75.) 2(25.0) 0(0.0)	0.351	Frequency 6 months Fast Slow	6(54.5) 5(45.5)	6(75.0) 2(25.0)	0.361
Background 12months Alpha Theta Delta	5(50.0) 3(30.0) 2(20.0)	6(100.0) 0(0.0) 0(0.0)	0.113	Frequency 12months Fast Slow	6(54.5) 5(45.5)	6(100.0) 0(0.0)	0.049*
Epileptiform pattern at Presentation Generalized Focal-generalized None	12(92.3) 1(7.7) 0(0.0)	4(50.0) 0(0.0) 4(50.0)	0.016*	Slowing at Presentation Focal Generalized Intermittent None	1(7.7) 4(30.8) 7(53.8) 1(7.7)	0(0.0) 2(25.0) 2(25.0) 4(50.0)	0.147
Epileptiform pattern at 6 months Yes No	0(0.0) 9(100.0)	2(25.0) 6(75.0)	0.110	Slowing at 6 months Focal Generalized Intermittent None	- 2(22.2) 6(66.7) 1(11.1)	- 2(25.0) 4(50.0) 2(25.0)	0.713
12month Focal Generalized	- -	- -		Slowing at 12months Focal	2(22.2)	2(33.3)	0.405

Focal-generalized None	- -	- -		Generalized Intermittent None	6(66.7) 1(11.1)	2(33.3) 2(33.3)	

4.53 Socio-biological Characteristics of 21 Patients Treated with Levetiracetam or Carbamazepine at Olabisi Onabanjo University Teaching Hospital a in South Western Nigeria over a period of one year

Of the 21 participants that developed SIS/SIE, 12(57.1%) were males and 9(43.9%) were females ($p<0.195$). The socio-demographic, clinical characteristics, and MR of participant with seizures only that are on CBZ were statistically comparable to those on LEV except for MR at 12months ($p\leq0.028$), CSID at 12months ($p\leq0.045$), CSID at 24months ($p\leq0.012$) and MR at 24month ($p\leq0.014$).

Table 73: Socio-biological Characteristics of 21 Patients Treated with Levetiracetam or Carbamazepine at Olabisi Onabanjo University Teaching Hospital a in South Western Nigeria over a period of one year

Variables	CBZ	LEV	p value
Age Mean(SD)	54.46±14.75	57.25±11.42	0.654
Gender Male N(%) Female N(%)	 6(46.2) 7(53.8)	 6(75.0) 2(25.0)	 0.195
NIHSS at 1month Not severe Severe	 9(69.3) 4(30.8)	 6(75.0) 2(25.0)	 0.304
NIHSS at 1year Not severe Severe	 9(69.3) 4(30.7)	 8(100.0) 0(0.0)	 0.361
MRS at 1 month Good outcome N(%) Poor outcome N(%)	 6(46.2) 7(53.80	 6(75.0) 2(25.0)	 0.195
MRS at 1 year Good outcome N(%) Poor outcome N(%)	 8(61.5) 5(38.5)	 6(75.0) 2(25.0)	 0.525
Mortality at 1 month N(%)	2(15.4)	0(0.0)	0.243
Mortality at 1 year N(%)	3(23.1)	0(0.0)	0.142
CSID AT 1month CI n(%) NCI n(%)	 13(100.0) 0(0.0)	 4(50.0) 4(50.0)	 0.005*
CSID at 1year CI n(%) NCI n(%)	 8(80.0) 2(20.0)	 4(50.0) 4(50.0)	 0.180

Table 74: Socio-biological Characteristics of 21 Patients Treated with Levetiracetam or Carbamazepine at Olabisi Onabanjo University Teaching Hospital a in South Western Nigeria over a period of one year

Variables	CBZ	LEV	p value
NIHSS at 2years Not severe Severe	 8(66.6) 4(33.4)	 6(75.0) 2(25.0)	 0.797
MRS at 2 years Good outcome N(%) Poor outcome N(%)	 7(58.3) 5(41.7)	 4(50.0) 4(50.0)	 0.714
Mortality at 2 years N(%)	3(23.1)	2(25.0)	0.920
CSID at 2years CI NCI	 7(77.8) 2(22.2)	 2(33.3) 4(66.7)	 0.085

4.54 Socio-biological Characteristics of 85 Stroke Patients with Stroke Induced Seizure and Stroke Induced Epilepsy Treated at University College Hospital Ibadan for a period of two years

Of the 85 stroke patients recruited from FMCA, 39(45.9%) were males while 46(54.1%) were females. A total of 66(78%) had ischasemic stroke while 19(22%) had haemorrhagic stroke. A total of 30(35%) developed seizure disorder following stroke. Of the 66 participants with ischaemic stroke, 25(38%) developed seizures whereas seizure was recorded among 5 of the 19 individuals who had haemorrhagic stroke, (38% vs 26%).

Furthermore, 55(64.7%) of the participants had no seizure, of the 30 patients that developed seizure 8(9.4%), 5(5.9%), and 17(20.0%) had seizures only, seizure to epilepsy and epilepsy only respectively.

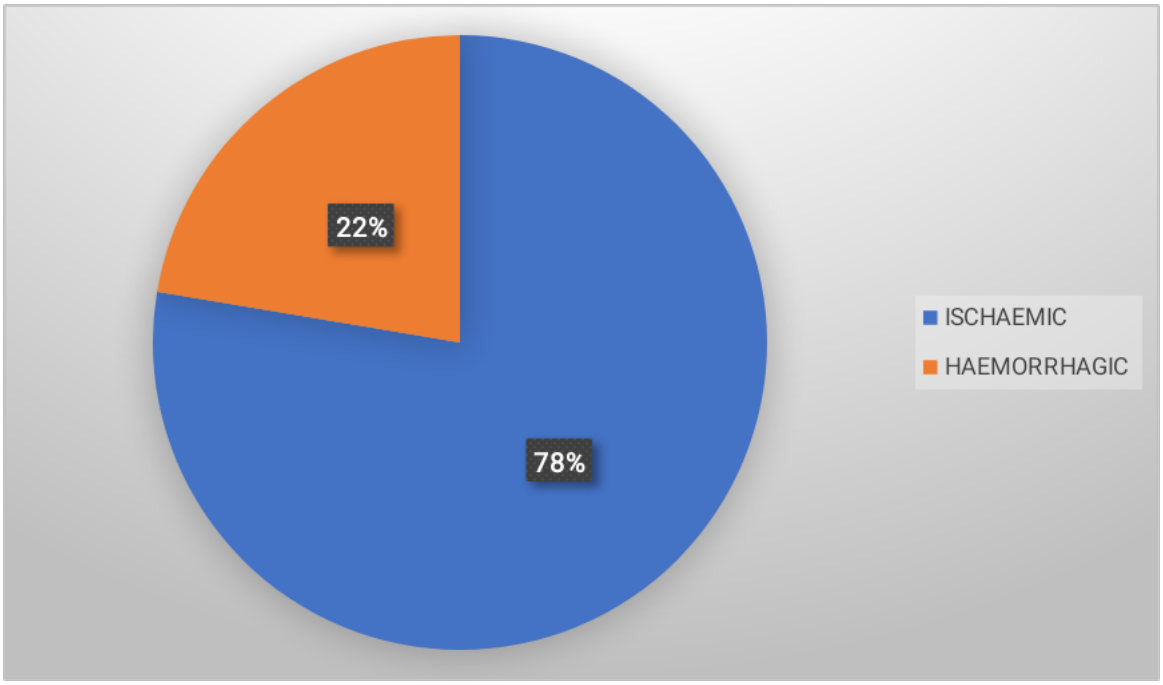


Figure 25: Stroke classification based on type among 85 cohorts Treated at University College Hospital Ibadan in South Western Nigeria for a period of two years

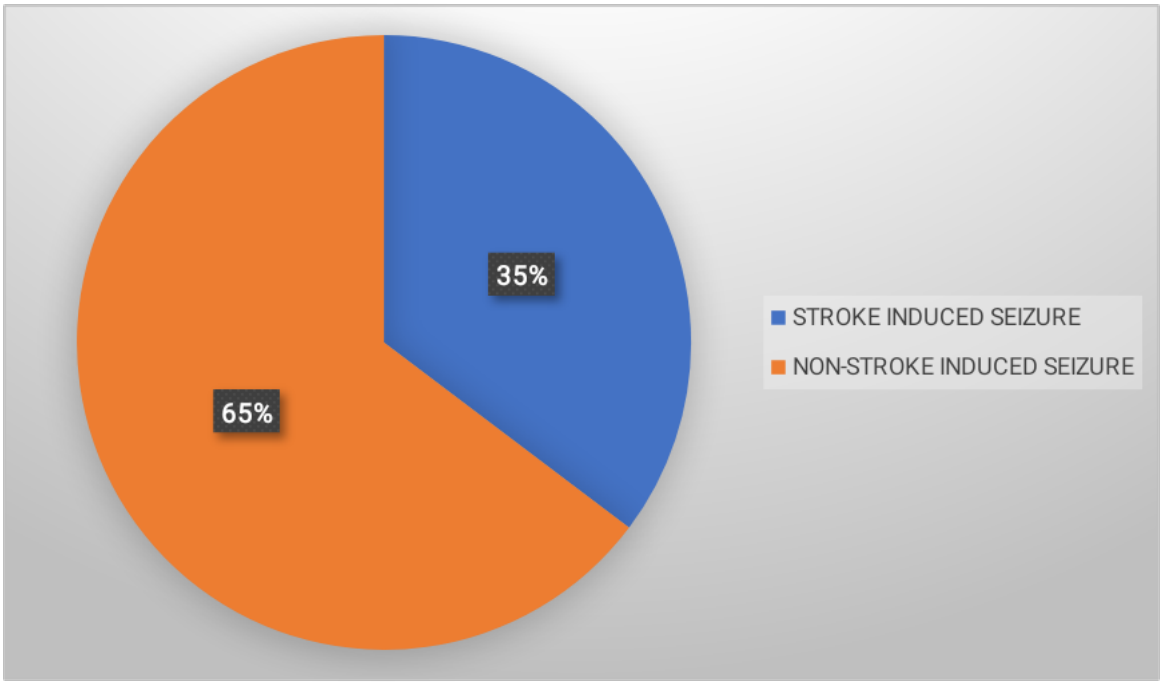


Figure 4.26: Stroke classification based on Seizure Occurrence/presence of Seizure among Post-Stroke Seizure and NSIS Patients Treated at University College Hospital Ibadan in South Western Nigeria for a period of two years

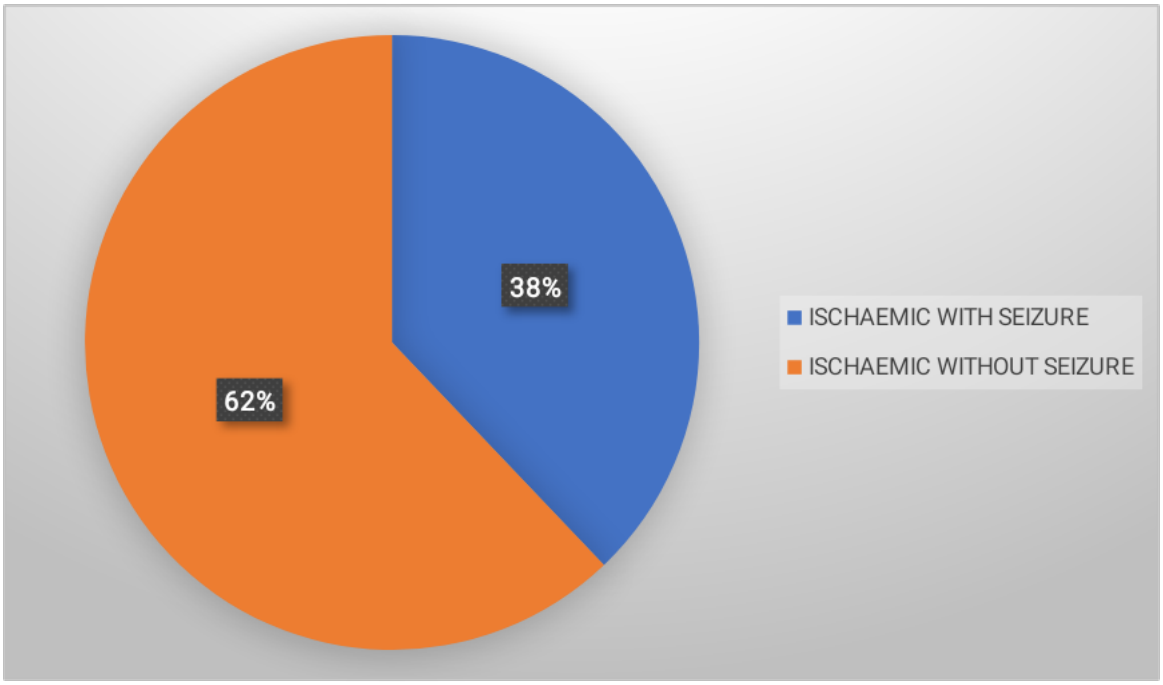


Figure 4.27: The Frequency of Haemorrhagic Stroke Participants with Stroke Induced Seizure and Non-Stroke Induced Seizure Treated at University College Hospital Ibadan in South Western Nigeria for a period of two years

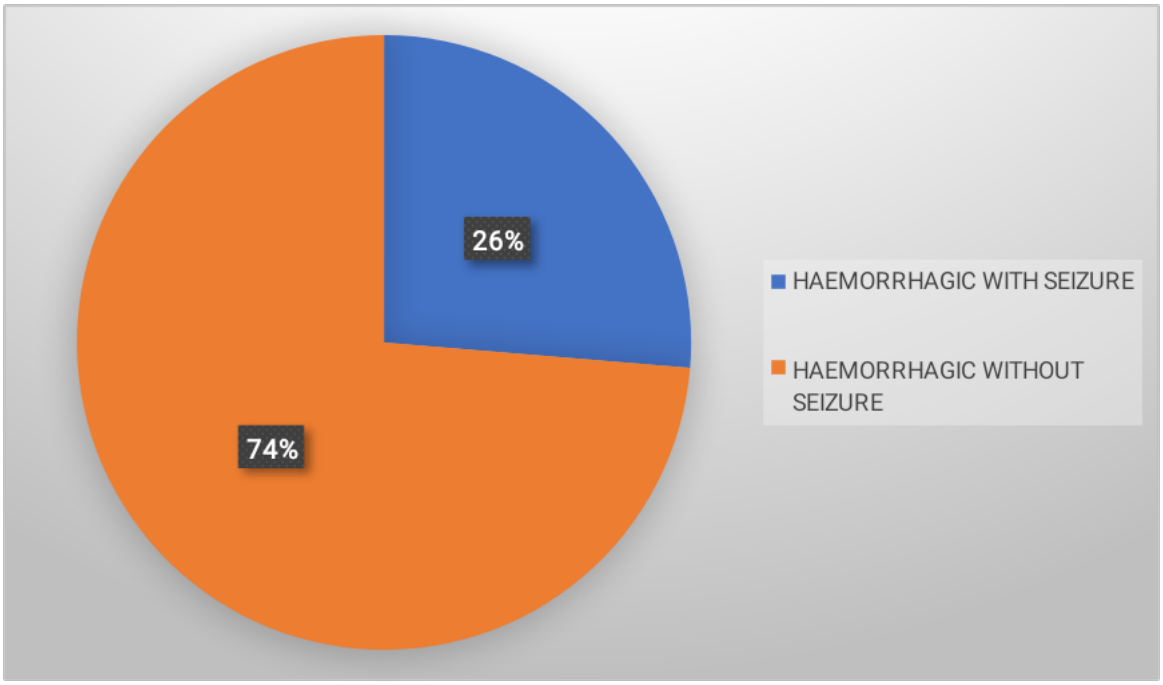


Figure 4.28: The Frequency of Ischaemic Stroke Participants with Stroke Induced Seizure and Non-Stroke Induced Seizure Treated at University College Hospital Ibadan in South Western Nigeria for a period of two years

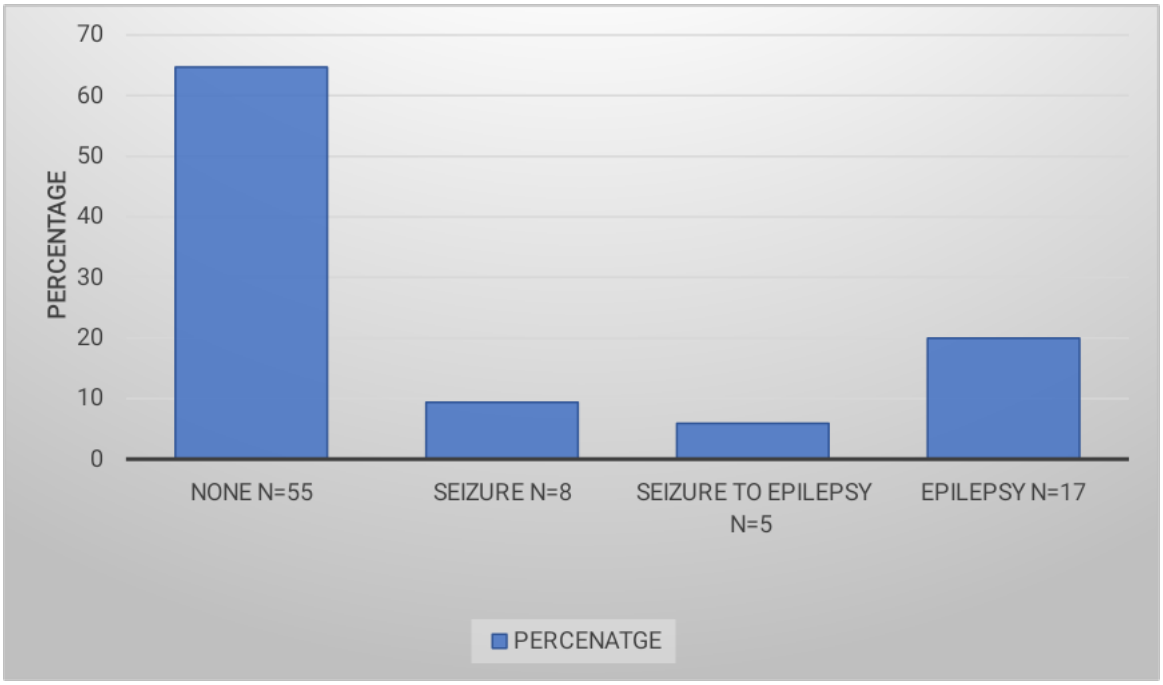


Figure 4.29: Frequency of Seizure and Epilepsy among Stroke Patients Treated at University College Hospital Ibadan in South Western Nigeria for a period of two years

4.55 Comparison of Clinical characteristics of Stroke Survivors with or without Seizure treated at University College Hospital Ibadan for a period of two years.

Patterns of stroke location revealed that there were higher number of participants with ischemic stroke at parietal lobe [38(57.6%) vs 0(0.0%); p <0.001], temporal lobe [14(21.2%) vs 0(0.0); p<0.028], lower number of participants at lentiform [4(6.1% vs 6(31.6%); p<0.002], and lower thalamus [4(6.1%) vs 8(42.1%); p<0.001], respectively compared to hemorrhagic stroke.

Majority of the participants had stroke in the MCA region with 43(65.2%) as ischemic and 7(36.8%) as hemorrhagic (p<0.027). Among participants with PCA, 9(13.6%) were ischemic while 11(57.9%) were hemorrhagic stroke (p <0.001).

Table 75: Comparison of Clinical characteristics of Stroke Survivors with or without Seizure treated at University College Hospital Ibadan for a period of two years.

Variables	Ischaemic n= 101	Haemorrhagic n = 39	Total N=140	x^2 Value	p Value
A. Clinical Characteristics					
Gender n (%) Male Female	30(45.5) 36(54.5)	9(47.4) 10(52.6)	39(45.9) 46(54.1)	0.022	0.883
Stroke Severity n (%) Minor stroke Moderate stroke Moderate to severe Severe stroke	4(7.5) 20(37.7) 14(26.4) 15(28.3)	0(0.0) 9(47.4) 6(31.6) 4(21.1)	4(5.6) 29(40.3) 20(27.8) 19(26.4)	2.169	0.538
Hypertensive n(%) Anti-hypertensive n(%)	57(86.4) 45(68.2)	19(100.0) 19(100.0)	76(89.4) 64(75.3)	2.898 2.898	0.089 0.089
Diabetics n(%) Anti-diabetics n(%)	20(30.3) 9(13.6)	2(10.5) 0(0.0)	22(25.9) 9(10.6)	3.008 2.898	0.083 0.089
Statin n(%)	11(16.7)	1(5.3)	12(14.1)	1.582	0.208
Mass effect n(%)	3(4.5)	12(63.2)	15(17.6)	34.87	0.000
Raised ICP n(%)	10(15.9)	7(36.8)	17(20.7)	3.906	0.048
Aspiration pneumonia n(%)	10(15.9)	5(26.3)	15(18.3)	1.065	0.302
PTE n(%)	2(3.2)	2(10.5)	4(4.9)	1.700	0.192
B. Location					
Basal ganglia n(%) Caudate Lentiform	5(7.7) 4(6.1)	1(5.3) 6(31.6)	6(7.1) 10(11.8)	0.131 9.255	0.718 0.002

Lobar Involvement n(%)					
Frontal Lobe	30(45.5)	5(26.3)	35(41.2)	2.231	0.135
Parietal Lobe	38(57.6)	0(0.0)	38(44.7)	19.78	0.000
Temporal Lobe	14(21.2)	0(0.0)	14(16.5)	4.83	0.028
Occipital Lobe	6(9.1)	1(5.3)	7(8.2)	0.286	0.593
Subcortical n(%)					
Internal Capsule	10(15.2)	5(26.3)	15(17.6)	1.27	0.261
Thalamus	4(6.1)	8(42.1)	12(14.1)	15.81	0.000
Infratentorial n(%)					
Cerebellum	2(3.1)	2(10.5)	4(4.8)	1.80	0.180
Brain stem					
Pons	3(4.5)	0(0.0)	3(3.5)	0.895	0.344
Midbrain	3(4.5)	0(0.0)	3(3.5)	0.895	0.344
Cortical Involvement n(%)					
Cortical	17(25.8)	2(10.5)	19(22.4)	1.97	0.160
No cortical	49(74.2)	17(89.5)	66(77.6)	1.97	0.160
Age grouped					
<35	3(4.5)	2(10.5)	5(5.9)	0.98	0.613
36-70	47(71.2)	13(68.4)	60(70.6)		
71-95	16(24.2)	4(21.1)	20(23.5)		
C. Arterial Territory					
ACA n(%)	14(21.2)	2(10.5)	16(18.8)	1.102	0.294
MCA n(%)	43(65.2)	7(36.8)	50(58.8)	4.881	0.027
PCA n(%)	9(13.6)	11(57.9)	20(23.5)	16.06	0.000

4.56 Mortality Rate Among 140 Participants Treated at University College Hospital Ibadan for a period of two years.

The mortality rate among stroke cohort was 12.9%, 41.2%, 41.2%, 52.9%, 54.1%, and 56.5% at 7 days, 1 month, 3 months, 6 months, 12 months, and 24 months, respectively. Furthermore, mortality rate was higher among hemorrhagic stroke cohort compared to ischemic stroke cohort from 7 days to 24 months and these were consistently statistically significant.

Table 76: Mortality Rate Among 140 Participants Treated at University College Hospital Ibadan for a period of two years

Variables	7days	1months	3months	6months	12months	24months
Stroke Patient n(%)	11(12.9)	35(41.2)	35(41.2)	45(52.9)	46(54.1)	48(56.5)
Ischaemic n(%)	8(12.1)	27(40.0)	27(40.9)	34(51.5)	34(51.5)	36(54.5)
Haemorrhagic n(%)	16(84.2)	8(42.1)	8(42.1)	11(57.9)	12(63.2)	12(63.2)
SIS n(%)	3(10.0)	8(26.7)	8(26.7)	10(33.3)	10(33.3)	10(33.3)
Seizure type						
ISPWS n(%)	1(4.0)	6(24.0)	6(24.0)	7(28.0)	7(28.0)	7(28.0)
HSPWS n(%)	2(40.0)	2(40.0)	2(40.0)	3(60.0)	3(60.0)	3(60.0)

4.57: Comparison of Sociodemographic Clinical Characteristics among 25 Ischemic Stroke Patients and 5 Hemorrhagic Stroke Patients with Stroke Induced Epilepsy

Among 30 patients that developed SIE, 17(56.7%) were males and 13(44.3%) were females. There were 25(83.3%) ischemic and 5(26.3%) hemorrhagic stroke participants that developed SIE. The mean age of participants with SIE among ischemic stroke patients is 59.32±15.24 compared to a value of 43.60±12.95 among hemorrhagic stroke patient with SIE and this attained a significant level ($p \leq 0.041$). The median stroke volume among participants with ischemic stroke with SIE is 8(39.0) compared to the value of 3.00(28.00) among those with hemorrhagic stroke with SIE and this was significant ($p \leq 0.147$).

Among those with PCA stroke with SIE, 2(8.0%) were ischemic compared to 4(80.0%) that had hemorrhagic stroke, and this was significant ($p<0.001$).

Furthermore, the presence of mass effect was more among hemorrhagic cohorts 3(60.0%) compared to 2(8.0%) among ischemic cohorts ($p \leq 0.004$)

Table 77: Comparison of Sociodemographic Clinical Characteristics among 25 Ischemic Stroke Patients and 5 Hemorrhagic Stroke Patients with Stroke Induced Epilepsy

Variables	ISPWS n=25	HMPWS n=5	x^2 value	p value
Gender n(%) Male Female	 15(60.0) 10(40.0)	 2(40.0) 3(60.0)	0.679	0.410
Age Mean (SD)	59.32(15.24)	43.60(12.95)	2.148	0.041
Stroke size Median (Range)	4.00(19.00)	10.00(20.00)	-1.409	0.170
Stroke volume cm^3 Median (Range)	8(39.00)	30.00(28.00)	-1.490	0.147
Cortical involvement n(%) Cortical No cortical	 8(32.0) 17(68.0)	 2(40.0) 3(60.0)	0.120	0.729
Hypertensive n(%)	18(72.0)	5(100.0)	1.826	0.177
Diabetics n(%)	14(56.0)	2(40.0)	0.429	0.513
ACA n(%)	3(12.0)	0(0.0)	0.667	0.414
MCA n(%)	20(80.0)	2(40.0)	3.409	0.065
PCA n(%)	2(8.0)	4(80.0)	13.50	<0.001*
Antihypertensive n(%)	18(72.0)	5(100.0)	1.826	0.401
Anti-diabetics n(%)	0(0.0)	1(25.0)	6.701	0.035*
Statin n(%)	7(28.0)	0(0.0)	1.826	0.177
Mass effect n(%)	2(8.0)	3(60.0)	8.112	0.004*

4.58 Comparison of Socio-biological Characteristics between Participants with Ischemic Stroke with or without seizure treated at University College Hospital Ibadan over a period of two years.

Of the 25(83.3%) participants with ischemic stroke, 27(27%) had SIS/SIE with 17(63.0%) males and 10(37.0%) females. 19(70.4%) of ischemic SIS/SIE used antihypertensive while 35(47.3%) of ischemic NSIS used antihypertensive (p≤0.040). Concerning use of statin, 19(70.4%) of ischemic SIS/SIE used statin while 25(33.8%) of ischemic NSIS used statin (p≤0.001). Again, presence of cortical involvement of cranial CT was higher 12(44.4%) in the ischemic stroke patients with SIS/SIE compared to 14(18.9%) NSIE (p≤0.009). The mean age of ischemic stroke patients with SIS/SIE was 67.41±11.96 compared to 61.58±9.74 among ischemic cohort with NSIS and this was statistically significant (p≤0.014).

Furthermore, there was a significant difference between ischemic cohort with SIS/SIE and NSIS with regards to raised ICP (p≤0.025) and PTE (p≤0.023).

Table 78: Comparison of Socio-biological Characteristics between Participants with Ischemic Stroke with or without seizure treated at University College Hospital Ibadan over a period of two years.

Variable n(%)	SIS/SIE n=25	NSIS n=41	Statistics	p-value
Gender Male Female	15(60.0) 10(40.0)	15(36.6) 26(63.4)	3.434	0.064
Mass effect	2(8.0)	1(2.4)	1.107	0.293
Antihypertensive	15(60.0)	16(39.0)	2.743	0.098
Anti-diabetics	5(20.0)	4(9.8)	1.384	0.239
Statin	9(36.0)	16(39.0)	0.060	0.806
Raised ICP	0(0.0)	10(24.4)	6.378	0.012*
Aspiration pneumonia	0(0.0)	10(24.4)	6.378	0.012*
PTE	0(0.0)	2(4.9)	1.108	0.292
UTI	0(0.0)	10(24.4)	6.378	0.012*
Hypertension	18(72.0)	25(61.0)	0.831	0.362
Diabetes mellitus	14(56.0)	6(14.6)	12.582	<0.001*
Cortical involvement Cortical Not cortical	8(32.0) 17(68.0)	9(22.0) 32(78.0)	0.820	0.365
ACA n(%)	3(12.0)	11(26.8)	2.044	0.153
MCA n(%)	20(80.0)	23(56.1)	3.908	0.048
PCA n(%)	2(8.0)	7(17.1)	1.086	0.297
AGE Mean(SD)	59.32(15.24)	63.54(14.30)	-1.133	0.261

NIHSS 0 Mean(SD	18.24(9.769)	17.05(6.618)	0.591	0.557
Stroke size	4.00(19.00)	3.00(39.00)	0.162	0.872
Stroke volume	8.00(39.00)	8.00(39.00)	0.178	0.859

Table 79: Comparison of Socio-biological Characteristics between Participants with Ischemic Stroke with or without seizure treated at University College Hospital Ibadan over a period of two years.

Variable n(%)	SIS/SIE	NSIS	Statistics	p-value
Background Alpha Theta Delta Intermixed fast	 8(32.0) 7(28.0) 9(36.0) 1(4.0)	 14(34.1) 12(29.3) 15(36.6) 0(0.0)	1.672	0.643
Epileptiform Focal Generalized Focal - generalized No	 3(12.0) 13(52.0) 2(8.0) 7(28.0)	 2(4.9) 17(41.5) 1(2.4) 21(51.2)	4.449	0.217
Slowing Generalized Intermittent No	 11(44.0) 5(20.0) 9(36.0)	 16(39.0) 8(19.5) 17(41.5)	0.214	0.899

4.59: Comparison of Socio-biological Characteristics between participants with Hemorrhagic Stroke with or without Seizure treated at University College Hospital Ibadan over the period of two years.

Of the 19 participants with hemorrhagic stroke, 5(26.3%) had SIS/SIE while 14(73.7%) had NSIS. Of the 19 hemorrhagic cohort with SIS/SIE, 2(40.0%) were males compared to 3(60.0%) females while hemorrhagic cohort with NSIS comprised 7(50.0%) males and 7(50.0%) females.

Table 80: Comparison of Socio-biological Characteristics between participants with Hemorrhagic Stroke with or without Seizure treated at University College Hospital Ibadan over the period of two years

Variable n(%)	SIS/SIE n=5	NSIS n=14	Statistics	p-value
Gender Male Female	2(40.0) 3(60.0)	7(50.0) 7(50.0)	0.148	0.701
Mass effect	3(60.0)	9(64.3)	0.029	0.865
Anti-diabetics	2(50.0)	0(0.00)	7.875	0.019*
PTE	0(0.0)	2(14.3)	0.798	0.372
UTI	0(0.0)	3(21.4)	1.272	0.259
Statin	0(0.0)	2(14.3)	0.798	0.372
Raised ICP	1(20.0)	6(42.9)	0.827	0.363
Aspiration pneumonia	0(0.0)	5(35.7)	2.423	0.120
Hypertension	5(100.0)	11(78.6)	1.272	0.258
Diabetes mellitus	2(40.0)	0(0.0)	6.259	0.012*
Cortical involvement Cortical Not cortical	2(40.0) 3(60.0)	0(0.0) 14(100.0)	6.259	0.012*
ACA n(%)	0(0.0)	2(14.3)	0.798	0.372
MCA n(%)	2(40.0)	5(35.7)	0.029	0.865
PCA n(%)	4(80.0)	7(50.0)	1.360	0.243
AGE Mean(SD)	43.60(12.95)	58.07(18.41)	-1.607	0.126
NIHSS 0 Mean(SD	14.20(2.49)	16.93(4.71)	-1.219	0.239
Stroke size	20.00(10.00)	12.00(8.00)	1.368	0.189
Stroke volume	28.00(30.00)	56.00(21.0	0.134	0.895

		0)		

4.60: Comparison of Socio-biological Characteristics and Mortality Rate among Non Stroke Induced Seizure and Stroke Induced Epilepsy (Seizure only, Seizures to Epilepsy, and Epilepsy only cohorts) treated at University College Hospital Ibadan over a period of two years.

Of the 85 participants recruited, 55(57.9%) had NSIS while 30(42.1%) had SIS. Of the 30(42.1%) with SIS, 8(26.7%) had seizure only, 5(16.7%) had seizure that progress to epilepsy, and 17(56.7%) had epilepsy only after stroke.

Table 81: Comparison of Socio-biological Characteristics and Mortality Rate among Non Stroke Induced Seizure and Stroke Induced Epilepsy treated at University College Hospital Ibadan over a period of two years.

Variables n(%)	None N=55	Seizures N=8	Seizures to Epilepsy N=5	Epilepsy N=17	P_1 Value	P_2 Value	P_3 Value
Gender Male Female	 22(40.0) 33(60.0)	 3(37.5) 5(62.5)	 1(20.0) 4(80.0)	 13(76.5) 4(23.5)	0.0338	0.893	0.009*
Stroke type Ischemic Hemorrhagic	 41(74.5) 14(25.5)	 6(75.0) 2(25.)	 3(60.0) 2(40.0)	 16(94.1) 1(5.9)	0.273	0.978	0.082
Age (Mean±SD)	62.15(15.46	62.75(15.08	59.60(10.83	53.00(17.05	0.202	0.918	0.041*
NIHSS 0, Mean(SD)	17.02(6.15	26.38(12.64	12.80(3.03	14.82(4.79	<0.001*	0.001*	0.182
Size, Median(range)	6.00(39.00)	5.00(13.00)	4.00(22.00)	4.00(19.00)	0.955	0.781	0.827
Volume in cm^3 Median(range)	12.00(61.50)	13.00(34.00)	12.00(34.00)	4.00(39.00)	0.698	0.467	0.473
Mass effects	10(18.20	1(12.50	1920.0)	3(17.60	0.981	0.692	0.960
Ventricular effacement	6(10.9)	0(0.0)	1920.0)	3920.0)	0.502	0.326	0.351
Raised ICP	16(29.1)	0(0.0)	0(0.0)	1(5.9)	0.065	0.159	0.049*
Hypertension	36(65.5)	8(100.)	5(100.0)	10(58.8)	0.071	0.047*	0.619
Diabetes	6(10.9)	7(87.5)	3960.0)	6(35.3)	<0.001*	<0.001*	0.018*
1month mortality	27(49.1)	7(87.5)	1(20.0)	0(0.0)	<0.001*	0.042*	<0.001*
3months mortality	27(49.1)	7(87.5)	1(20.0)	0(0.0)	<0.001*	0.042*	<0.001*
6months mortality	35(63.5)	8(100.0)	2(40.0)	0(0.0)	<0.001*	0.039*	<0.001*
12months mortality	35(63.5)	8(100.0)	2(40.0)	0(0.0)	<0.001*	0.047*	<0.001*

4.61: Patterns of Mortality among 85 Stroke Patients Treated at University College Hospital Ibadan over a period of two years.

Of the 85 participants, 66(77.6%) had ischemic stroke while 19(23.4%) had hemorrhagic stroke. However, out of the 85 ischemic stroke patients, 39(45.9%) were males and 46(55.1%) were females. Furthermore, of the 39 hemorrhagic stroke patients, 20.5%, 41.0%, 41.0%, 48.7%, 48.7%, and 48.7% died by 7days, 1 month, 3 months, 6 months, 12 months, and 24 months, respectively. On the other hand, 8.9%, 24.8%, 24.8%, 26.1%, 28.7%, and 31.7% died in the ischemic group. There were higher M:F [60(67.4%) vs 29(32.6%)], lower mean age [59.99±9.80 vs 65.39±11.77; p≤0.004], higher hemorrhagic death

Table 82: Patterns of Mortality among 85 Stroke Patients Treated at University College Hospital Ibadan over a period of two years.

Variable n(%)	Alive	Dead	Statistics	p value
Gender Male Female	21(58.8) 16(43.2)	18(37.5) 30(62.50	3.120	0.077
Age (Mean±SD)	59.60(10.83	53.00(17.05	0.202	0.320
Hypertension	22(59.5)	37(77.1)	3.057	0.080
Diabetics mellitus	9(24.3)	13(27.1)	0.083	0.773
Hyperlipidemia	5(13.5)	8(17.0)	0.195	0.659
Heart Disease	1(2.7)	2(4.2)	0.132	0.717
Stroke Type Ischaemic Haemorrhagic	30(81.1) 7(18.9)	36(75.0) 12(25.)0	0.445	0.505
NIHSS 0, (Mean±SD)	53.00(17.05	52.11(14.05	0.4448	0.072
ACA	5(13.5)	11(22.9)	1.209	0.272
MCA	24(64.9)	26(54.2)	0.987	0.320
PCA	9(24.3)	11(22.9)	0.023	0.897
Size, Median(range)	14.00(17.0)	13.00(139.0)	0.678	0.451
Mass Effect	5(13.5)	10(20.8)	0.770	0.380
Small Vessel Disease	10(35.7)	9(25.7)	0.739	0.390
Large Artery	6(21.4)	11(31.4)	0.790	0374

4.62: Predictors of Seizures and Epilepsy among 85 Stroke Patients Treated at University College Hospital Ibadan in South Western Nigeria over a period of two years

On regression analysis, only diabetes mellitus (Beta coefficient 3.474, odd ratio 7.261, p≤0.007, C.I 2.578-403.990) predicted SIS. However, also only diabetes mellitus (Beta coefficient 2.574, odd ratio 1.225, p≤0.036, C.I 1.190-114.691) predicted SIE.

Table 83: Predictors of Seizures and Epilepsy among 85 Stroke Patients Treated at University College Hospital Ibadan in South Western Nigeria over a period of two years

Variables	B	p-value	Odds ratio	95% CI
Seizures				
NIHSS	0.066	0.230	1.441	0.959-1.191
Hypertension	-17.331	0.998	0.000	0.000-
Diabetes mellitus	3.474	0.007*	7.261	2.578-403.990
Mortality 30days	0.412	0.790	0.071	0.073-31.205
Mortality 90days	0.412	0.790	0.071	0.073-31.205
Mortality 180days	-0.933	1.000	0.000	0.000-
Mortality 360days	-17.963	1.000	0.000	0.000-
Epilepsy				
Age mean	-0.060	0.057	3.634	0.885-1.002
Gender Male Female	 1.923 Reference	 0.058	 3.602	 0.939-49.882
Raised ICP	-1.985	0.168	1.889	0.008-2.331
Diabetes mellitus	2.574	0.036*	1.225	1.190-144.691
Mortality 30days	-0.125	1.000	0.000	0.000-
Mortality 90days	-0.215	1.000	0.000	0.000-
Mortality 180days	2.713	1.000	0.000	0.000-
Mortality 360days	17.838	1.000	0.000	0.000-

4.63: Comparison of EEG Characteristics among 30 Stroke Induced Epilepsy/ Stroke Induced Seizure (11 Carbamazepine versus 19 Levetiracetam) Treated University College Hospital Ibadan in South Western Nigeria over period of 2years

The frequency of alpha, theta, delta and intermixed fast were 1(12.5%), 5(62.5%), 1(12.5%) and 1(12.5%) respectively in the CBZ compare to 8(57.1%), 4(28.6%), 2(14.3%) and 0(0.0) respectively in LEV group. This is however not statistically significant (p≤0.149). Similarly, at 12months, the frequency of alpha, theta, and delta was 3(50.0%), 2(33.3%),and 1(16.7%), in the CBZ group compared respectively to 12(85.7%), 2(14.3%), and 0(0.0%) in the LEV group.

4.84: Comparison of EEG Characteristics among 41 Stroke Induced Epilepsy/ Stroke Induced Seizure (22 Carbamazepine versus 19 Levetiracetam) Treated at University College Hospital Ibadan in South Western Nigeria over period of 2years

Variable	CBZ N (%)	LEV N (%)	p value	Frequency	CBZ N (%)	LEV N (%)	p value
Background at Presentation				Frequency Presentation			
Alpha	1(12.5)	8(57.1)	0.129		2(18.2)	8(42.1)	0.180
Theta	5(62.5)	4(28.6)		Fast	9(81.8)	11(57.9)	
Delta	1(12.5)	2(14.3)		Slow			
Intermixed fast	1(12.5)	0(0.0)					
Background 6 months				Frequency			
Alpha	2(33.3)	12(85.7)	0.047*	6 months			
Theta	3(50.0)	2(14.3)		Fast	3(50.0)	12(85.7)	0.091
Intermixed slow	1(16.7)	0(0.0)		Slow	3(50.0)	2(14.3)	
Background 12months				Frequency 12months			
Alpha	3(50.0)	12(85.7)	0.149				
Theta	2(33.3)	2(14.3)		Fast	4(66.7)	12(85.7)	0.329
Intermixed slow	1(16.7)	0(0.0)		Slow	2(33.3)	2(14.3)	
Epileptiform pattern at Presentation				Slowing at Presentation			
Focal	1(9.1)	2(10.5)	0.431		-	-	0.081
Generalized	5(45.5)	11(57.9)		Focal	4(36.4)	9(47.4)	
Focal-generalized	0(0.0)	2(10.5)		Generalized	5(45.5)	2(10.5)	
None	5(45.50	4(21.1)		Intermittent	2(18.2)	8(42.1)	
				None			
Epileptiform pattern at 6 months				Slowing at 6 months			
Focal	0(0.0)	2(14.3)	0.510	Focal	-	-	0.594
Generalized	3(50.0)	6(42.9)		Generalized	1(16.7)	2(14.3)	
Focal-generalized	0(0.0)	2(14.3)		Intermittent	3(50.0)	4(28.6)	
None	3(50.0)	4(28.6)		None	2(33.3)	8(57.1)	
12month				Slowing at 12months			
Focal	0(0.0)	2(14.3)	0.273				
Generalized	3(50.0)	2(14.3)		Focal	-	-	0.805
Focal-generalized	0(0.0)	2(14.3)		Generalized	1(20.0)	2(14.3)	
None	3(50.0)	8(57.1)		Intermittent	2(40.0)	4(28.6)	
				None	2(40.0)	8(57.1)	

CBZ- Carbamazepine LEV – Levetiracetam

4.64 Socio-biological Characteristics of 30 Patients Treated with Levetiracetam or Carbamazepine at University College Hospital Ibadan in South Western Nigeria over a period of one year

Of the 30 participants that developed SIS/SIE, 17(54.8%) were males and 13(45.2%) were females ($p<0.346$). The socio-demographic, clinical characteristics, and MR of participant with seizures only that are on CBZ were statistically comparable to those on LEV except for NIHSS at 12months ($p\leq0.041$) and NIHSS at 24month ($p\leq0.040$).

4.85 Socio-biological Characteristics of 30 Patients Treated with Levetiracetam or Carbamazepine University College Hospital Ibadan in South Western Nigeria over a period of one year

Variables	CBZ n=11	LEV n=19	p value
Gender Male N(%) Female N(%)	 5(45.5) 6(54.5)	 12(63.2) 7(36.8)	 0.346
NIHSS at 1month Not severe Severe	 6(54.5) 5(43.5)	 6(100.) 0(0.0)	 0.145
NIHSS at 1year Not severe Severe	 4(36.4) 7(63.6)	 6(100.0) 0(0.0)	 0.041*
MRS at 1 month Good outcome N(%) Poor outcome N(%)	 4(36.4) 7(63.6)	 8(42.1) 11(57.9)	 0.757
MRS at 1 year Good outcome N(%) Poor outcome N(%)	 4(36.4) 7(63.6)	 12(63.2) 7(36.8)	 0.156
Mortality at 1 month N(%)	3(27.3)	5(26.3)	0.954
Mortality at 1 year N(%)	5(45.5)	5(26.3)	0.284
CSID AT 1month CI n(%) NCI n(%)	 10(90.9) 1(9.1)	 19(100.0) 0(0.0)	 0.181
CSID at 1year CI n(%) NCI n(%)	 5(83.3) 1(16.7)	 10(71.4) 4(28.6)	 0.573

*p<0.05 comparing CBZ and LEV CBZ- Carbamazepine LEV – Levetiracetam CI – Cognitively Impaired NCI – Non Cognitively Impaired

4.86 Socio-biological Characteristics of 30 Patients Treated with Levetiracetam or Carbamazepine at University College Hospital Ibadan in South Western Nigeria over a period of one year

Variables	CBZ	LEV	p value
NIHSS at 2years Not severe Severe	 3(30.0) 7(70.0)	 6(100.0)	 0.040*
MRS at 2 years Good outcome N(%) Poor outcome N(%)	 3(30.0) 7(70.0)	 12(63.2) 7(36.8)	 0.089
Mortality at 2 years N(%)	5(45.5)	5(26.3)	0.284
CSID at 2years CI NCI	 5(100.0) 0(0.0)	 4(50.0) 4(50.0)	 0.057

*p<0.05 comparing CBZ and LEV CBZ- Carbamazepine LEV – Levetiracetam CI – Cognitively Impaired NCI – Non Cognitively Impaired