ECG ABNORMALITIES AND ASSOCIATED FACTORS AMONG ADULT EPILEPSY PATIENTS AT JIMMA UNIVERSITY MEDICAL CENTER, JIMMA, ETHIOPIA: A CROSS SECTIONAL STUDY

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SUMMARY

Background: Epilepsy is a disease condition in which a person has recurrent seizures due to a chronic, underlying process. It affects approximately 50 million people worldwide and 4 million people in Sub-Saharan Africa. ECG abnormalities are one of the commonest comorbidities in epilepsy patients that increase mortality and morbidity of epilepsy patients.

Objective: The objective of this study is to evaluate ECG abnormalities and associated factors among adult epileptic patients having follow-up at JUMC adult seizure clinic in 2021G.C.

Methods: A hospital based cross sectional study was conducted on Patients presenting to adult seizure clinic at JUMC from November 1- January 30 2021 G.C. A standard 12 lead resting ECG was recorded for participants of the study. The data was collected by two trained nurses and analyzed using SPSS version 26. Binary logistic regression analysis was done to measure possible associations between ECG abnormality and independent factors. A P value of <0.05 cut off point and AOR with 95%CI was considered to declare a statistically significant association.

Results: The mean age of the participants of the study was 32.2 with Majority of the patients were in the age group 20-29. Male accounted for 60.2% and females 39.8% of the study participants. Abnormal ECG occurred in 82 (43.2%) patients. The most common ECG abnormality identified was early repolarization pattern. The identified associated factors with abnormal ECG was male sex with specific adjusted ratio of (AOR) of 4.751 and 95% CI (.273, .933) , p=0.029.

Conclusions: There is a high frequency of ECG abnormalities among epilepsy patients and hence routine ECG should be performed for early detection and management of fatal arrhythmias and a close follow up in those who have ECG markers of sudden cardiac death.

Key Words: Epilepsy, ECG abnormality, Arrhythmia, ECG, Seizure, SCD, SUDEP

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LIST OF ABBREVIATIONS

JUMC -- Jimma University Medical Center

ECG – Electrocardiogram

EEG -- Electroencephalogram

AED -- antiepileptic drug

SUDEP -- Sudden Unexpected Death in Epilepsy

SCD -- Sudden Cardiac Death

AAD -- Anti Aarrytmic drug

TWA -- T Wave Alteration

VT -- Ventricular Tachycardia

VF – Ventricular Fibrillation

AF -- Atrial Fibrillation

GTCS -- Generalized Tonic Clonic Seizure

SE -- Status Epilepticus

CHF -- Congestive Heart Failure

ILAE- International League Against Epilepsy

HR -- Heart Rate

CI -- Confidence Interval

HRV-- Heart Rate Variability

LQT -- Long QT

OR-- Odds Ratio

ERP -- Early Repolarization Pattern

SD -- Standard Deviation

DALY -- Disability Adjusted Life Years

ER – Early repolarization

ERP – Early Repolarization Pattern

TWA—T Wave Alterans

LMIC -- Low to Middle Income Countries

HIC -- High Income Countries

WHO – World Health organization

SCD – Sudden Cardiac Death

RAD – Right Axis Deviation

LAD – Left Axis Deviation

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CHAPTER ONE – INTRODUCTION

1.1 BACKGROUND OF THE STUDY

Epilepsy describes a disease condition in which a person has risk of recurrent seizure due to a chronic underlying process where as seizure is a transient occurrence of signs or symptoms due to abnormal excessive or synchronous neuronal activity in the brain [1]. According to the 2017 International League against Epilepsy classifications seizure can be classified as .Generalized onset, Focal Onset, Unknown and Unclassified [2].

The diagnosis of Epilepsy can be established clinically as well as with the use of EEG (electroencephalogram). Clinical diagnosis of epilepsy requires two or more unprovoked seizure occurring > 24 hours apart. Diagnosis based on EEG requires distinct EEG seizure activity during the clinically evident event (i.e. abnormal repetitive rhythmic activity having a discrete onset and termination) [3].

Electrocardiogram is a graphic representation of electrical activity of the heart. Resting standard 12 lead ECG is the most common, widely used and available mode detecting electrical activity of the heart. ECG is the basis for diagnosis of normal as well as abnormal electrical activity (arrhythmia). ECG also plays vital role in diagnosis of structural heart diseases [3].

Abnormal ECG is ECG recording of heart rhythm that is not of normal range for rhythm, rate, axis, P wave, QRS duration, PR interval, QT interval, T wave and ST Segment. Abnormal ECG may result from abnormalities of electrical impulse generation, conduction or both. The causes of arrhythmias are structural heart and nonstructural heart diseases that alter the generation and conduction of cardiac impulse [4].

Etiological factors of cardiac arrhythmias in patients with epilepsy are grouped into three. These are (1) acute and chronic effect of seizure on heart (2) shared CVD risk factors and (3) epilepsy treatment related. Convulsive seizure exerts pro arrhythmic effect by altering the autonomic nervous system and cardiac fibrosis due to repeated seizures-induced hypoxemia and cardio toxic effect of excess catecholamine. Shared risk factors for both epilepsy and cardiac arrhythmia include inherited and acquired conditions like LQT syndrome that affects channels which are

expressed both in heart and brain. The third group (epilepsy treatment related) etiologies are particularly related to AEDs that act by blocking sodium channels in brain and heart [5].

The primary prevention of epilepsy mainly targets on the epidemiologically preventable etiologies of epilepsy. The prevention Task Force of the international League against Epilepsy, (also adapted by WHO) targets on 4 preventable etiologic categories of epilepsy: (1) perinatal insults, (2) traumatic brain injury (3) central nervous system infection, (4) stroke which have a potential to decrease 25% of the overall epilepsy burden [6].

1.2 STATEMENT OF THE PROBLEM

According to a report from 2016 Global Burden of Disease, about 50 million people suffer from epilepsy globally. Nearly 80% of people with epilepsy reside in LMIC. It accounts for >13 million Disability Adjusted Life Years (DALYs) and is responsible for 0.5% of the total disease burden. The burden of idiopathic epilepsy was highest in eastern, western, and southern sub Saharan Africa [7]. A report from Journal of Global Health shows the prevalence of epilepsy in Sub-Saharan Africa estimated to affect 5.4 million people [8]. In Ethiopia the highest prevalence of epilepsy was found in Zay society, the prevalence rate being 29.5 per 100 [9].The incidence of epilepsy in central Ethiopia was found to be 64 per 100,000 inhabitants annually. The corresponding rate for males was 72 and 57 for females. Head trauma was the most common possible etiologic factor identified [10].

Various studies support that epilepsy patients have a higher risk of developing structural cardiac abnormalities. [11]They have higher levels of left ventricular stiffness, left ventricular filling pressures and greater left atrial volume as determined by echocardiography than non–epileptic patients. [12, 13] The hearts of epilepsy patients tend to have higher left ventricular filling pressure, end systolic diameter and end systolic volume [14]. Increased serum levels of cardiac troponin I, indicative of myocardial injury, have been reported in ~25% of GTCS [15-17]. In addition ischemic heart disease is reported to be 1.9-fold more common among patients with epilepsy than in the general population [18].

Abnormal ECG patterns and arrhythmias are one of the most common comorbid medical conditions in patients with epilepsy, occurring in around 9% of epilepsy patients. The occurrence of these abnormal ECG in patients with epilepsy heightens mortality both in inpatient and outpatient settings. Abnormal ECG is one of the predictors of mortality in epilepsy patients that mandates therapeutic intervention [18, 19].

People with epilepsy are 24 times more at risk experiencing sudden cardiac death. This was demonstrated by The Seminal Amsterdam Resuscitation Studies which revealed the risk of cardiac arrest to be 2.8-fold greater in patients with epilepsy (and in symptomatic epilepsy cases was 5.8-fold greater than in the general population [20, 21]. In The Oregon Sudden Unexpected Death Study, patients with epilepsy succumbed to sudden cardiac arrest at an earlier age, 55 ± 25

years, than those without epilepsy, who died suddenly at 63 ± 19 years. Cardiac arrhythmias are the most common cause of sudden cardiac arrest and death [22].

The most common cause of death in patients with epilepsy is sudden unexpected death from epilepsy(SUDEP) [23, 24]. One of the proposed mechanisms for SUDEP is various ECG abnormalities and arrhythmias precipitated by seizure discharges acting via the autonomic nervous system, prolonged QT interval and tachyarrhythmia. ECG markers for cardiovascular arrhythmia and sudden death (T-Wave Alterans, ventricular late potentials) are more prevalent in patients with epilepsy [25, 26]. ECG abnormalities can identify patients at risk of SCD and SUDEP. These abnormal ECG markers of sudden cardiac death are Prolonged QT interval, early repolarization pattern and brugada pattern of ECG occur at increased frequency in patients with epilepsy [27].

Anti-epileptic drugs particularly carbamazepine and phenytoin act on sodium channels that are expressed in neurons and heart. Both are known to be pro-arrhythmic drugs and it is recommended to evaluate the ECG of a patient before initiation and escalating the dose of these AEDs to prevent cardiac electrical disturbance [28, 29]. Being old anti-epileptic drugs and cheap, sodium channel blocking AEDs are the most frequently used anti-epileptic drugs in low income countries including Ethiopia. But the cardiac burden, magnitude of arrhythmia these drugs pose in epilepsy patients is not well studied.

There is a high rate of occurrence of syncope in epilepsy patients. This is because syncope mimics epilepsy. The rate of diagnosing syncope via ECG in epilepsy patients reach as high as 41%. The routine use of ECG and evaluation for cardiac arrhythmia and abnormal ECG pattern enables to pick cardiogenic syncope and fatal arrhythmias. Studies done on epilepsy patients have shown that abnormal ECG detection helped in management of syncope in epilepsy patients. [30-33].Yet it is a common scenario that epilepsy patients in our settings are not worked up for syncope. This mandates the need to study the burden of abnormal ECG pattern that defines syncope in our patents.

ECG abnormalities and arrhythmias in epilepsy patients can be prevented by identifying patients at risk of developing it, by routine reviewing ECG, and instituting appropriate management for the detected abnormalities [34, 35]. Furthermore, in management of epilepsy, the concept of

“epileptic heart” is recently introduced. It aims at medical and device-based therapies to decrease cardiac electrical instability and thereby reduce life-threatening arrhythmias in at-risk individuals with chronic epilepsy [36].

The standard 12 lead ECG is the first line tool to assess cardiac rhythm disturbance. International guidelines on management of epilepsy recommend routine ECG recording for all epilepsy patient epilepsy as part of long term follow up care. The 12-lead standard ECG is a low-cost screening test for assessing fatal abnormal ECG markers SCD risk. Unfortunately it is quite common in our setting that patients are not worked up as part of the routine care. The burden of ECG abnormalities has remained unstudied. Hence, studying the prevalence of abnormal ECG and associated factors in epilepsy will be of paramount importance.

1.3 SIGNIFICANCE OF THE STUDY

Assessing prevalence of ECG abnormalities and associated factors in patients with epilepsy provide information regarding the burden of arrhythmia in epilepsy patients. It will also be helpful to influence the practice of physicians and other health care professionals with regard to routine and regular use of ECG which helps to identify epilepsy patients at risk of developing fatal cardiac arrhythmias. This further helps for improvement of services and quality of care provided at Jimma University Medical Center.

There are no previous studies done on this topic at JUMC. So the study will be a baseline for further studies on related topics. It can also be used as a reference tool for development of applicable guidelines. As to the knowledge of the primary investigator no study has been done regarding cardiac arrhythmia and abnormal ECG in epilepsy patients in Ethiopia. Hence, it will be very good entry for large scale studies at the country level.

CHAPTER TWO

2.1 LITERATURE REVIEW

2.1.2 PREVALENCE OF ECG ABNORMALITIES IN EPILEPSY PATIENTS

The connection between heart and brain is well known for years. Cardio-cerebral disease is the term that refers to disease conditions affecting both heart and brain. Epilepsy is one of the disease entities that fall under this group. ECG abnormalities are one of the commonest type of cardiac condition affecting the heart in patients with epilepsy. The prevalent type of abnormal ECG is varies depending upon the situation where the ECG is taken. For example the most common type of arrhythmia during ictal phase (during active seizure) is ictal asystole and post ictal phase (a time period immediately after seizure) is post ictal asystole. Other common arrhythmias in during ictal and post-ictal period are ictal bradycardia, ictal atrioventricular (AV) conduction block, postictal AV-conduction block, postictal atrial flutter/atrial fibrillation and postictal ventricular fibrillation [37].

This study will be done in epilepsy patients who visit adult seizure follow-up clinic of JUMC (not actively seizing patient), Hence, the study will be on clinic visiting patients during inter-ictal phase.

In a cross sectional study that involved 376 patients diagnosed with epilepsy showed that 28% of females and 14% of males had ECG abnormalities. Atrial Fibrillation was more frequent in female group whereas bradycardia and respiratory Sinus arrhythmia was higher in male group. Atrial fibrillation was more frequent in female group whereas bradycardia and respiratory sinus arrhythmia was higher in male group one patient had a potentially fatal asystole. for whom a pacemaker was inserted [38].

In a hospital based cross-sectional study done involving 101 patients with idiopathic epilepsy in Iran, 23.8% of patients had abnormal ECG. From the ECG analysis PVC occurred in 5 patients, PAC in 4 patients, Second AV block in 3 patients, Sinus bradicardia, Sinus Tachycardia, Significant Sinus arrhythmia, Sick sinus syndrome, AF, Long QT were identified in one patient for each arrhythmias described [39].

In a hospital based cross-sectional study that was undertaken in Egypt on 120 epilepsy patients diagnosed with epilepsy of GTCS type seizure, it was revealed that the mean PR interval was 147ms, mean QT interval of 362.8ms, QTc 42.5ms [40].

In a cross-sectional study that aimed at assessing ECG abnormalities in epilepsy patients that marks increased risk of sudden cardiac death involving 185 patients showed brugada pattern in three patients, severe QTC prolongation in 10 patients, ERP 62% [41].

A cross sectional hospital based study that involved 1000 epilepsy patients showed that 142 (14.2%) have repolarization abnormalities. Significantly affected patients were older patients and patients with poor seizure control. The study concluded that ECG has to be estabilished as part of work up for epilepsy patients [42].

A cross-sectional study that involved 338 patients with epilepsy in ambulatory EEG/ECG monitoring high-risk cardiac arrhythmias were detected in 18 (5.3%) patients while low-risk arrhythmias or negative studies were found in the others [43].

2.1.2 FACTORS ASSOCIATED WITH ECG ABNORMALITIES IN PATIENTS WITH EPILEPSY

In a cross sectional study that involved 1000 epileptic patients showed that repolarization ECG abnormalities are associated with older age and poor seizure control. The study concluded that ECG should be established as part of diagnostic work up of epilepsy in order to identify electrocardiographic early repolarization pattern abnormalities [42].

A prospective cross-sectional study that involved patients who were only on carbamazepine monotherapy showed that carbamazepine monotherapy does not have any significant effect on ECG time interval on short or long term variability [44]. But A cross-sectional study that involved 120 patients with the aim of assessing ECG abnormalities in patients who were on AEDs showed that ST-T abnormalities were frequently seen in patients who were using AEDs. The researchers concluded that polytherapy with sodium channel blocking AEDs was associated with brugada type ST elevation ECG abnormality [45].

A cross sectional study that involved patients with diagnosis of definite epilepsy, with the aim of assessing determining factors of ECG abnormalities in patients with epilepsy showed that older increasing age, male sex and polytherapy with antiepileptic were associated with altered ECG. The researchers finally concluded that routine ECG should be requested in these groups of patients to identify patients having increased risk of fatal ECG abnormalities [46].

A cross-sectional study that evaluated cardiac repolarization indices in epilepsy patients with generalied tonic-clonic seizure treated with carbamazepine and valproic acid showed that carbamazepine using males and valproaic acid using females were associated increased risk of ventriculary arrhythmias [47].

A retrospective case-cross over study that involved data from inpatient and ED Databases in California with aim of assessing whether an epilepsy or status epilepticus encounters were associated with subsequent encounter for cardiac arrhythmia; history of status epilepticus was associated with subsequent cardiac arrhythmia and cardiac arrest over multiple chronic time frames [48].

In a prospect cross-sectional case control study that involved 336 epilepsy patients and age sex matched controls in Japan showed that male gender was associated with abnormal ECG repolarization pattern [49].

A comparative cross sectional study done on inter-ictal ECG of patients with drug resistant epilepsy showed that drug resistance epilepsy was associated with significant ECG abnormalities. The study further identified that duration of QRS was correlated with epilepsy duration [50].

Most studies done are in developed countries, no study has been done with regard to prevalence and associated factors of ECG abnormalities in patients with epilepsy in Ethiopia. Furthermore most of the studies focused only on specific abnormal ECG patterns and did not consider the effect of recent (last) seizure, family history of epilepsy on development of abnormal ECG. This study will consider the effect of last seizure on ECG of epileptic patients and aims at assessing all possible clinically relevant ECG abnormalities.

2.2 CONCEPTUAL FRAMEWORK

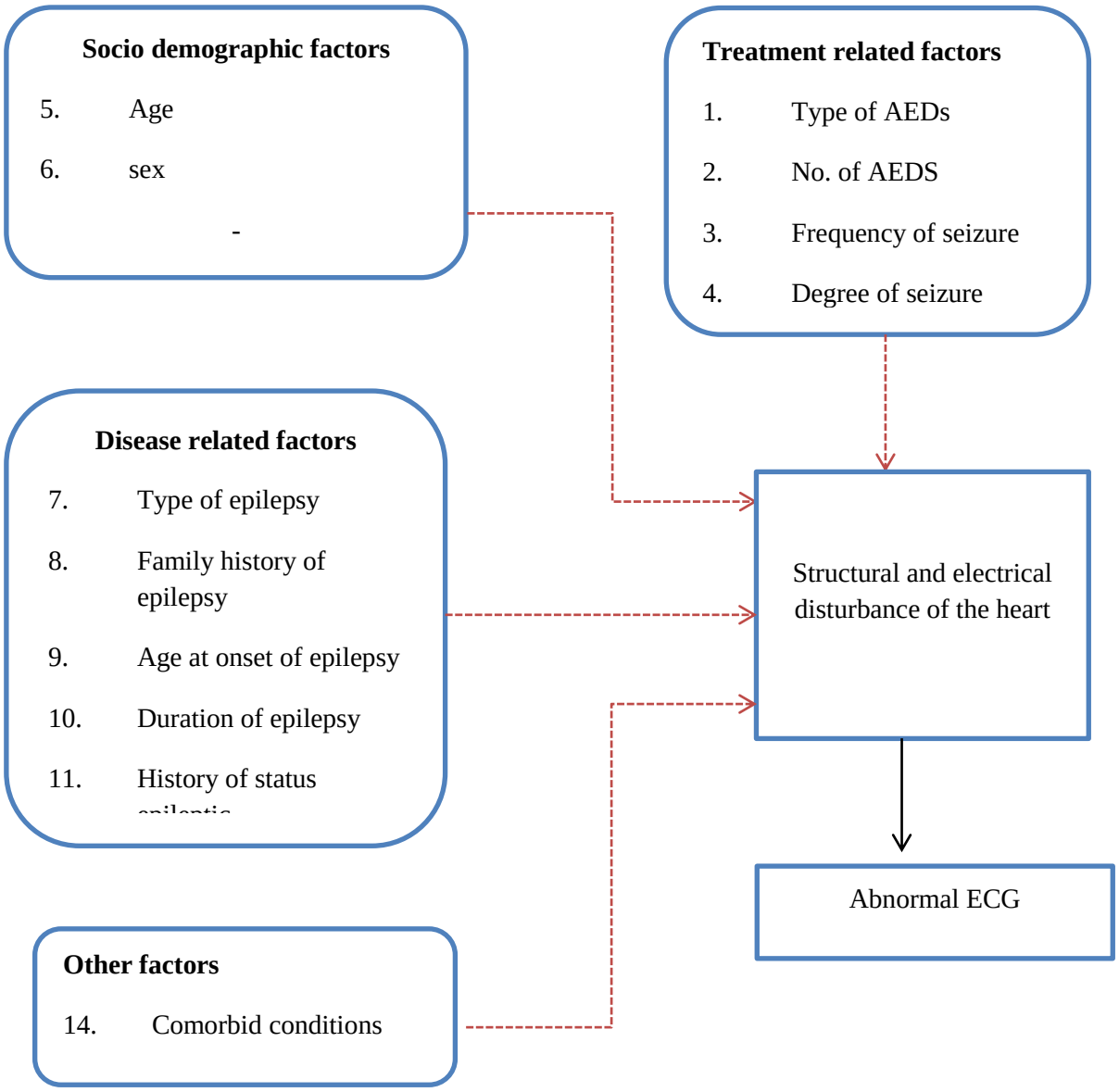

Figure 1: Conceptual framework of ECG abnormality and associated factors among patients with epilepsy, at adult chronic follow up seizure clinic of Jimma University Medical center, Jimma, Ethiopia, 2021

CHAPTER THREE: OBJECTIVES

3.1 GENERAL OBJECTIVES

To determine ECG abnormalities and associated factors among epileptic patients at adult chronic follow up, seizure clinic of Jimma University Medical Center, Jimma, Ethiopia, 2021 G.C.

3.2 SPECIFIC OBJECTIVES

- To determine the prevalence of ECG abnormalities at adult chronic follow up seizure clinic of Jimma University Medical Center, Jimma, Ethiopia, 2021 G.C.
- To describe baseline characteristics of epileptic patients at adult chronic follow up seizure clinic of Jimma University Medical center, Jimma, Ethiopia, 2021 G.C.
- To determine factors associated with ECG abnormalities among epileptic patients at adult chronic follow up seizure clinic of Jimma University Medical center, Jimma, Ethiopia, 2021 G.C.

CHAPTER FOUR: METHOD AND MATERIALS

4.1 STUDY AREA AND PERIOD

The study was conducted at Jimma University Medical Center. .Geographically JUMC is located in Jimma town, 352 km southwest of Addis Ababa. The town has 2 government hospitals, 3 heqlth centers and is also home for different higher educational institutions.

The department of Internal Medicine is one of the departments which provides both inpatient and outpatient services. The inpatient services are organized in to general medical wards and units. Chronic illness follow up is one of the OPD services provided by the department. In adult chronic illness follow up clinic seizure clinic runs every Thursday. There are 1500 patients with diagnosis of epilepsy having regular follow up at JUMC adult follow up clinic.

The study was conducted from November 1, 2021 GC – January 30, 2022 GC.

4.2 STUDY DESIGN

A hospital-based cross sectional study will be employed.

4.3 SOURCE POPULATION

All Patients with confirmed epilepsy or possible epilepsy by clinical examination aged greater than 18 years, able to undergo ECG recording as judged by the physician and having follow up between November 1, 2021 GC – January 30, 2022 GC at JUMC adult seizure follow up clinic.

4.4 STUDY POPULATION

All patients who had follow up at adult seizure clinic visiting the OPD between November 1 2021 G.C. and January 30 2022 G.C. who had confirmed epilepsy or possible epilepsy, whose age is above 18 years, able to undergo ECG recording as judged by the physician, who are not seizing, not critically ill, not using anti-arrhythmic drugs, non-febrile patients . The patients are included until the required sample size is obtained.

4.4.1 INCLUSION CRITERIA

Patients having follow up at seizure clinic and meet the criteria to be labeled as confirmed epilepsy or possible epilepsy by clinical examination.

- Patients whose age >18
- able to undergo ECG recording as judged by the physician

4.4.2 EXCLUSION CRITERIA

- Seizing patient
- Critically ill patients
- Using antiarrhythmic drugs
- Fever > 103degree Fahrenheit

4.5 SAMPLING

4.5.1 SAMPLE SIZE

No sampling technique was used. All epilepsy having follow-up at adult seizure clinic were i that fulfill inclusion criteria were be enrolled during the study period

4.5.2 SAMPLING TECHNIQUE

Consecutive sampling of clients coming to the clinic on their appointment dates was conducted from list of card number of epilepsy patients on follow up at JUMC adult seizure clinic within the study period drawn from a logbook. Every consecutive patient who fulfills inclusion criteria was included during the study period.

4.6 MEASUREMENTS

4.6.1 VARIABLES

Independent Variables

- Age
- Sex
- Type of epileptic seizure
- Degree of seizure control /frequency of seizure
- Number of anti-epileptic drugs
- Duration of epilepsy
- Age at the onset of epilepsy
- Type of anti-epileptic drugs
- Comorbid medical illnesses
- Duration of AED therapy
- Family history of epilepsy

-History of Status epilepticus

Dependent variables

-Abnormal ECG

4.6.2 DATA COLLECTION PROCEDURES

A Checklist was used and filled by reviewing the patients chart and interviewing the patient. The check list was provided initially in English language and was translated to native languages (Amharic and Afaan Oromo) by bilingual translators. The checklist includes the socio-demographic characteristics of the patients, clinical characteristics. An ECG machine from the department of internal medicine at adult follow up clinic was used to record ECG of the patient.

Data on the prevalence of ECG abnormalities was collected by a physician who recorded 12 lead resting ECG following the standard ECG recording procedure. Data regarding socio-demographic characteristics and associated factors of ECG abnormality in epilepsy was collected by one nurse working at seizure clinic by careful review of the patient's chart and asking the client using the prepared checklist and questionnaire. The overall activity was supervised by the principal investigator. Training of data collectors was done in order to have a common understanding of the data collection tools and improve the quality of data.

4.7 DATA QUALITY CONTROL

Before the actual data collection pre-testing of the data collection instrument was held ahead of data collection at adult seizure follow-up clinic of Jimma University Medical Center. After the pretest, the necessary amendment of tool was done for the final data collection.

Data collectors were trained intensively for two days on the overall study design, objective of the study and data collection procedure.

The Primary investigator checked the collected data for completeness and corrective measures wias taken accordingly. The collected data was cleaned, coded and explored before analysis. Besides this, the investigator carefully entered and cleaned the data before the commencement of the analysis.

4.8 DATA PROCESSING AND ANALYSIS

The collected data was checked, coded, and entered in to Epi-Data version 3.1 and analyzed using software program SPSS 26. Descriptive analysis was carried out using frequency

distributions, central tendency and dispersion measures. Presence of statistical association between dependent and independent variables was assessed using Binary logistic regression, multicollinearity and model fitness test. Adjusted Odds Ratio with 95% Confidence interval was used to measure strength of association. Variables with $p \leq 0.05$ was considered as statistically significant. Results are presented in text, tabulation and figurative presentations from which conclusions and recommendations was made. In addition, results was also compared with other studies and discussed.

4.9 ETHICAL CONSIDERATION

Before conducting the study, permission and approval letter from JUMC ethical review committee was obtained for accessing patient's recorded data. An official letter was obtained from department of internal medicine and was given to responsible body at chronic illness follow up clinic. Cooperation letter was obtained from Jimma University Institute of Health. The data was collected after taking full verbal consent of participants after providing adequate information about the research. During the data collection procedure, the patient's privacy and confidentiality was kept to the maximum.

4.10 DISSIMINATION PLAN

After research completion and finalizing report, it will be submitted to department of internal medicine, Jimma University Medical Center, the Ministry of Health and other concerned institutions and stake holders for possible application and publication of the study.

4.11 OPERATIONAL DEFINITIONS

Possible Epilepsy ;- According to the International League Against Epilepsy (ILAE), epilepsy is defined by any of the following conditions: (1) at least 2 unprovoked seizures occurring >24 h apart;

Anti-arrhythmic drugs: medications or drugs prescribed by health personnel and doesn't include traditional and alternative medicines.

Illiterate – can't read and write and haven't attend formal education

Anti-epileptic drug treatment- medications or drugs prescribed by health personnel and doesn't include traditional and alternative medicines.

Poly-pharmacy- taking at least two prescribed medications for at least one disease condition and which doesn't include temporary drugs like analgesics , antibiotics of short duration (doesn't include anti TB) and other over the counter drugs.

Income –estimated average amount of cash money an individual earns monthly in terms of Ethiopian currency. For those without monthly salary their raw materials will be estimated in terms of Ethiopian birr.

Critically ill patients – Patients who are unable to communicate because of severe illness, those with abnormal vital signs which need urgent interventions and patients who sustain seizure while waiting for their turn or at the time of clerking.

Chronic illnesses- Long standing disease conditions which includes HIV/AIDS, TB, DM, CKD, CLD

ECG markers of sudden cardiac death:- Long QT syndrome Short QT syndrome Brugada syndrome Early repolarization syndrome Fragmented QRS Idiopathic VF WPW, Complete AV block

State of seizure control:- excellent, if the patient had ≤ 1 attack in year; good, if he ≥ 2 attacks in year; acceptable, if ≤ 1 attack in month and unacceptable, > 1 attack in month

Anti-arrhythmic drug – drugs used to treat arrhythmias like beta blockers, calcium channel blockers, digitalis.

Abnormal ECG: abnormal rate, rhythm, axis, conduction, repolarization. For the purpose of this study ECG reading parameters as summarized below in the table. The criteria for each specific type of arrhythmia pattern will be based on standard criteria for diagnosis.

Table1:- Definition of summary of common ECG abnormalities with their standard criteria

ECG ABNORMALITIES	DESCRIPTION OR DEFINITION
Sinus rhythm	Regular RR intervals: between 600-1000 ms where Every P wave is followed by a QRS complexes

TACHYCARDIA AND TACHYARRHYTHMIA (RR INTERVALS < 600 MS)	
Tachycardia with narrow QRS complexes (<120 ms)	Regular RR intervals: sinus tachycardia, atrioventricular nodal re-entry tachycardia, atrial flutter Irregular RR intervals: atrial fibrillation
Tachycardia with wide QRS complexes (>120 ms	Regular RR intervals: sinus tachycardia with pre-existing aberrant conduction Regular or irregular : sinus tachycardia with pre-existing aberrant conduction RR intervals: ventricular tachycardia, ventricular flutter Ventricular fibrillation without organized QRS complexes
BRADYCARDIA AND BRADYARRHYTHMIA (RR INTERVALS > 1000 MS)	
Bradycardia	Wide QRS complexes and regular RR intervals: sinus bradycardia with pre-existing aberrant conduction, ventricular escape rhythm Narrow QRS complexes and irregular RR intervals: atrial fibrillation, sick sinus Narrow QRS complexes and regular RR intervals: sinus bradycardia (sick sinus, sleep), atrioventricular block
Bradycardia Due to atrioventricular (AV) block	2nd degree AV-block Type I (Wenckebach): PR interval gradually increases until one QRS complex is blocked Type II (Mobitz): PR interval normal, but not every P wave is followed by QRS complex (2:1, 3:1, …) 3rd degree AV-block:complete block, AV dissociation
CONDUCTION INTERVAL ABNORMALITIES	

PR interval	PR interval >200 ms: 1st degree AV-block PR interval <120 ms (plus 'delta wave'): pre-excitation syndrome (Wolff-ParkinsonWhite syndrome
Wide QRS complex (> 120 ms	Left bundle branch block (LBBB): RsR' in V6 Right bundle branch block (RBBB): RsR' in V1 Intraventricular conduction delay: not RBBB or LBBB
REPOLARIZATION ABNORMALITIES	
QT interval	QT intervals depend on sex, age and heart rate (Need to be corrected with formulas)
QT interval prolongation	Corrected QT intervals (Fridericia) >465 ms in women and >457 ms in men, when heart rate 60-99 bpm
QT interval shortening	short QT syndromes with corrected QTc <320 ms
QT dispersion (QTd)	Difference between shortest/longest QT interval on 12-lead ECG
T-wave alternans (TWA)	Beat-to-beat alternation of morphology/amplitude of ST segment/T-wave
ST SEGMENT ABNORMALITIES	
ST elevation	Abnormal like Pattern seen ST elevation Elevated in myocardial infarction, pericarditis, left ventricular hypertrophy, early repolarization infarction: Elevation>0.1 mV in limb leads or >0.2 mV in

	precordial leads
ST depression	Abnormal >0.1 mV in V5-V6, or >0.15 mV in AVF or III
Negative T wave	Not the same polarity as the QRS completx

The following ECG reference values (corrected with Fridericia's formula) will be used when appropriate**.**

Table 2:- Summary of normal range for common ECG parameter measurements

ECG PARAMETER	**CORRECTED VALUE**
P wave	≤ 80 m
PR interval	120-200 ms
QRS complex	80-120 m
ST segment	≤ 0.1 mV mV/0.2 mV (40 ms after J point limb/precordial leads)
QTc interval	374 - 465 ms (females), 368 - 457 ms (males)
RR interval	600 - 1000 ms (Heart rate 60 - 100 bpm)

.(Adapted from :Epileptic Disord, Vol. 23, No. 1, February 2021)

CHAPTER FIVE: RESULTS

5.1 SOCIODEMOGRAPHIC CHARCTERSTICS

A total of 190 epilepsy patients were included in the study. Among these 115 (60.2%) were males and 75 (39.8%) were females. The mean age of the study group was 32.2 years with SD of 11.8 years. Majority of the study participants were between 20-29 accounting for 66 patients (34.%), followed by 30-39 years accounting for 56 (29.3%). Most of the respondents were below age of 60 accounting for 95.3% and the remaining were above 60 years, 9(4.7%). Majority of the respondents were Muslims accounting for 123 (64.4%) followed by orthodox and protestant religion followers which account for 46 (24.1%) and 20 (10.5%) respectively (Table 3).

Table 3:- Socio demographic characteristics epilepsy patients at JUMC adult seizure follow up clinic, Jimma, Ethiopia, 2021 G.C.

Variable		Frequency	Percent
Age	5 - 19 years	22	11.5%
	20- 29 years	66	34.6%
	30- 39 years	56	29.3%
	40 - 49 years	31	16.8%
	50 - 59 years	6	3.1%
	60 - 69 years	7	3.7%
	>70	2	1%
Sex	Male	115	60.2%
	Female	75	39.8%
Religion	Muslim	123	64.4%
	Orthodox	45	24.1%
	Protestant	20	10.5%
	Others	2	1%
Ethinicity	Oromo	133	69.6%
	Amhara	23	12.6%
	Gurage	3	1.6%
	Dawuro	14	7.3%
	Yem	14	7.3%
	Others	3	1.6%
Marital Status	Single	79	41.4%
	Married	98	51.8%
	Divorced	11	5.8%
	Widowed	2	1%
Educational Status	Illiterate	58	30.4%
	Read and write	9	4.7%
	Primary education	69	36.1%
	Secondary education	34	18.3%
	Diploma	11	5.8%
	Degree	8	4.2%
	Postgraduate	1	0.5%
Occupation	Government Employee	20	10.5%
	Merchant	10	5.2%
	Student	38	19.9%
	Daily Laboror	20	10.5%
	Farmer	52	27.2%
	House Wife	29	15.2%
	Other	21	11.5%
Residence	Urban	93	49%
	Rural	97	51%

5.2 CLINICAL CHARACTERSITICS OF EPILEPSY PATIENTS

For most of the participants of the study epilepsy was diagnosed above 20 years of age which account for 76 (40%) of the respondents. With regard to duration of epilepsy, 83.3% (160) of the respondents have reported to live with epilepsy more than 10 years. With regard to anti-epileptic therapy, 189 (99.5%) of the patients were on anti-epileptic therapy. Only one patient was not on AED. Majority of the patients were on 119 (62.6%) Monotherapy (taking one AED) and the remaining 71(36.9%) were on polytherapy of AEDs. Majority of the respondents have uncontrolled epilepsy. This accounts for 120 (63.2%) of patients. Most patients (92.1%) had no other comorbid medical conditions. The etiology of epilepsy in majority of the patients is unknown which accounts for163 (85.9%). The presumed cause of epilepsy is known in only 27 (14.2%) patients. (head trauma=25 patients, brain tumor and stroke one patient each) Most of the respondents had no family history of epilepsy and history of status epileptius which accounts for 92.7% and 98.3% of the participants of the study respectively (Table 4).

Table 4: clinical Characteristics of epilepsy patients at JUMC adult seizure follow up clinic, Jimma, Ethiopia, 2021 G.C.

Clinical characteristics	*Category*	*Frequency*	*Percent*
Age at the onset of epilepsy	<5	15	7.9%
	6-14	41	21.6%
	15-19	58	30.5%
	>20	76	40%
Duration of epilepsy	<5	52	27.4%
	6-10	44	23.2%
	>10	93	48.9%
Type of epilepsy	Generalized	164	85.9%
	Focal	27	14.1%
Taking AED?	Yes	190	99.5%
	No	1	0.5%
	Monotherapy	115	60.2%
	Polytherapy	69	36.1%
Degree of seizure control	Controlled	70	36.8%
	Uncontrolled	120	63.2%
Comorbid medical conditions	Yes	15	7.9%
	No	176	92.1%
Etiology of Epilepsy	Known	27	14.1%
	unKnown	163	85.9%
Family history of Epilepsy	Yes	14	7.3%
	No	177	92.7%
History of status epilepticus	Yes	9	4.7%
	No	182	95.3%

5.3 BLOOD PRESSURE AND PULSE RATE DISTRIBUTION OF EPILEPSY PATIENTS

Majority of the patients have normal systolic blood pressure and diastolic blood pressure. As can be seen from the mean systolic blood pressure is 117 mmHg with standard deviation of 15.1 mmgh and the mean diastolic blood pressure is 82.2 mmHg with standard deviation of 56.5 mmgh. Majority of the patients had normal pulse rate 60-100 which accounts for 172 (90.1%) of the patients (Table 5).

Table 5: frequency of blood pressure and heart rate among epilepsy patients at JUMC adult seizure follow up clinic, Jimma, Ethiopia, 2021 G.C.

Vital sign		*Frequency*	*Percent*	*Mean*	*SD*
Systolic Blood Pressure	<100	25	13.1%	117	15.1
	100-119	85	44.5%		
	120-139	62	32.5%		
	140-159	16	8.4%		
	>160	3	1.6%		
Diastolic blood pressure	<60	5	2.6%	82.2	56.5
	60-79	97	50.8%		
	80-89	64	33.5%		
	90-100	21	11%		
	>100	4	2.1%		
Pulse Rate	<60	7	3.7%	86.9	51.7
	60-100	172	90.1%		
	>100	11	5.8%		

5.3 ECG ANALYSIS AMONG EPILEPSY PATIENTS

Most patients (86.4%) had normal ventricular rate (60-100). The mean ventricular rate was 75 beat per minute with the SD of 11.8. Majority (88.5%) of patients had normal QRS duration. Majority of the patients (88.5%) had normal axis. The mean QRS duration is 89.06 with SD of 10.5. Most of participants of the study had normal PR interval that accounts for 93.7% of the patients with mean value of 151.5ms and SD of 24.8 (Table 6).

Table 6: Machine generated (Rate, interval, axis and duration) ECG analysis of epilepsy patients at JUMC adult seizure follow up clinic, Jimma, Ethiopia, 2021 G.C.

ECG Findings		Frequency	Percent	Mean	SD
Rate	<60	17	6.2%	75	11.8
	60-100	165	86.4%		
	>100	2	1%		
QRS Axis	Normal	169	88.5%	59.9	59.3
	LAD	7	3.7%		
	RAD	15	7.9%		
PR interval	Normal	179	93.7%	151.5	24.8
	Short	6	3.1%		
	Prolonged	6	3.1%		
QRS duration	Normal	157	82.2%	86.06	10.5
	Wide	3	1.6%		
	Narrow	31	16.2%		
QTc interval	Normal -	189	99%	395	45.1
	Short	-	-		
	Prolonged	2	1%		

FREQEUENCY OF ABNORMAL ECGS

The overall analysis of ECG of the participants of the study shows that 43.2% had abnormal ECG while the rest(56.8%) had normal ECG. The most common identified abnormal ECG pattern was Early repolarization which was seen in 20 patients followed by sinus bradycardia (15) RAD (15) (Table 7).

Table 7: Frequency of ECG specific abnormalties among epilepsy at JUMC adult seizure follow up clinic, Jimma, Ethiopia, 2021 G.C.

Abnormal ECG Pattern		*Frequency*	*Percent*
General ECG pattern	*Normal*	*82*	*43.2%*
	Abnormal	*108*	*56.8%*
Early repolarization pattern		20	10.5%
Sinus bradycardia		15	8.9%
RAD		15	8.9%
Nonspecific ST, TWAVE abnormality		13	5.3%
Sinus arrhtythmia		11	5.8%
Chamber enlargement (atrial and ventricular)		8	4.2%
LAD		7	3.7%
1st degree AV block		6	3%
LONG PR		6	3.2%
SHORT PR		6	3.2%
Old myocardial infarction (Q-waves)		5	2.6%
Non-specific ventricular conduction block		5	2.6%
Wide QRS		3	1.6%
PAC		2	0.5%
PVC		2	1%
Sinus tachycardia		2	1%
Prolonged QT		2	1%
Atrial fibrillation		1	0.5%
Junctional rhythm		1	0.5%

NB: One patient may have more than one abnormal ECG.

ECG MARKERS OF SCD AMONG EPILEPSY PATIENTS

Among ECG patterns that are known to pose increased risk of SCD only 10.5% of the study subjects had those markers of SCD. ERP (early repolarization pattern) occurred in Long QT twenty patients whereas long QT occurred in two patients (Table 8).

Table 8: ECG markers of SCD among epilepsy patients at JUMC adult seizure follow up clinic, Jimma, Ethiopia, 2021 G.C.

ECG markers of SCD	NUMBER	PERCENT
Short QT	0	0%
Long QT	2	1%
Brugada ECG	0	0%
VF/VT/WPW	0	0%
COMPLETE AV BLOCK	0	0%
ERP	20	10.5%

5.3 FACTORS ASSOCIATED WITH ECG ABNORMALITIES IN EPILEPSY PATIENTS

To see possible factors associated with occurrence of abnormal ECG among epilepsy patients bivariate analysis was done to identify covarities for the multivariale model using binary logistic regression method. In the bivariate analysis, the candidate variables having p-value<0.25 were selected for the final model (Table 9).

Table 9: ECG Pattern Changes and Associated Factors by Bivariate analysis and chi square test among epilepsy Patients.

	Group	Abnormal ECG –No (%)	Normal ECG-No (%)	Total	P-Value
Age	under 20	12 (6)	10 (5.2)	22 (11.6)	0.55
	20-39	50 (26.3)	71 (37.3)	121 (63.7)	
	40-59	15 (7.9)	23 (12.1)	38 (20)	
	above 60	5 (2.6)	4 (2.1)	9 (4.7)	
Sex	Male	56 (29.4)	58 (30.5)	114 (60))	0.02
	Female	26 (13.7)	50 (26.3)	76 (40)	
Educational Status	Formal	57 (30)	66 (34.7)	123 (64.5)	0.28
	Informal	25 (13.1)	42 (22.1)	67 (35.3)	
Residence	Urban	38 (20)	56 (29.5)	94 (49.5)	0.468
	Rural	44 (23.1)	52 (27.4)	96 (50.5)	
Age at onset of epilepsy	below 20	50 (26.3)	64 (33.7)	114 (60)	0.88
	20-39	26 (13.7)	39 (20.5)	65 (34.2)	
	40-59	5 (2.6)	5 (2.6)	10 (52.6)	
	above 60	1 (0.5)	0 (0)	1 (0.5%)	
Duration of epilepsy	< 5 year	29 (15.3)	23 (12.1)	52 (27.4)	0.03
	6-10 years	13 (6.8)	31 (16.3)	44 (23.2)	
	> 10 year	40 (20.5)	54 (28.4)	93 (48.9)	
Type of epilepsy	Focal	11 (5.8)	15 (7.9)	26 (13.7)	0.925
	Generalized	71 (37.4)	93 (48.9)	164 (86.3)	
Therapy	monotherapy	49 (25.8)	67 (35.3)	116 (61.1)	0.829
	polytherapy	32 (16.8)	41 (21.6)	73 (38.4)	
Family history of epilepsy	Yes	7 (3.7)	7 (36.8)	14 (7.4)	0.59
	No	75 (39.5)	101 (53.2)	176 (92.6)	
Status epilepticus	Yes	5 (2.6)	4 (2.1)	9 (4.7)	0.5
	No	77 (40.5)	104 (54.7)	181 (95.2)	
Comorbidity	Yes	7 (3.7)	9 (4.7)	16 (8.4)	0.96
	No	75 (39.5)	99 (53.1)	174 (91.6)	
Seizure control	Controlled	27 (14.2)	43 (22.6)	70 (36.8)	0.33
	Uncontrolled	55 (28.9)	65 (34.2)	120 (63.2)	

Hence two variables (Sex, duration of epilepsy) were identified as the expected factors associated with the development of abnormal ECGs. Hence multivariate analysis (binary logistic regression with enter methods) were used to identify the associated factor and the result is shown below with AOR value (Table 10)

Table 10: ECG Pattern Changes and Associated Factors by Binary Logistic Regression among epilepsy patients at JUMC adult seizure follow up clinic 2021 G.C

Variables	**AOR**	**(95% CI)**	**P value**
Sex	4.751	(2.73, .933)	0.029
Duration of epilepsy (>10 years)	0.461	(.384, 7.170)	0.497

Finally the variable Sex, with p-value less than 0.05 fitted the final model with AOR 4.751 (95% CI: .384, 7.170) identified as the associated factors with abnormal ECG pattern among Epilepsy patients (Table 10)

5.4 DISCUSSION

The study showed that sex ratio of M: F was 1.5:1 Mean age of the participants of the study was 32.2 years. Majority of the study groups were in the age range of 20 – 40 years. Majority of the patients were diagnosed with epilepsy for the first time by the age above 20 years which account for 40% of the patients.

Abnormal ECG occurred in 43.2% of patients. The study done in Iran showed that abnormal ECG findings occurred 23.8% of the patients [39]. The discrepancy can be explained by the small number of sample size in the later as well as the by the fact that the later study took only idiopathic epilepsy into consideration.

This study showed that 34.2% of females and 49.2% of males had abnormal ECG. This shows a higher proportion of abnormal ECG when compared to the study done [38] which showed 14% of males and 28% females had abnormal ECG. This discrepancy can explained by the fact that the later study was done in EEG monitoring unit of epilepsy as a diagnostic work up and limited range abnormalities that were included as Abnormal ECG.

This study showed that twenty two patients had markers of SCD. Twenty (10.5%) of these had ERP while two patients had prolonged QTc. While the study done in Netherland showed that 62% of epilepsy patients had ERP and 10 patients had prolonged QTc which is higher than the finding in our study [41]. This can be explained by the fact that the study involved epilepsy patient who were diagnosed to have refractory epilepsy. Yet, the prevalence of ERP in the study done in Egypt study is comparable to our finding [42].

The most common ECG abnormality identified in this study is Early repolarization pattern (ERP) which occurred in 20 patients. Sinus bradycardia occurred in 15 patients, sinus arrhythmia was seen in 11 patients. RAD was identified in 15 patients. The mean PR and QT interval is 151.5ms and 395 ms which comparable to the study done in USA [40].

Abnormal ECG pattern was associated in male This finding is comparable with the study done in Japan [49].

Abnormal ECG was associated in with sex male in this study while the study done in Egypt was mainly associated older age and poor seizure control [42]. The discrepancy might be due to small

number of sample size in this study. While the study done in Brazil showed that abnormal ECG was associated with increasing age, male sex and poly-therapy [46]. The discrepancy in the association might be due to that study involved a confirmed cases Epilepsy using EEG while the diagnosis of epilepsy in our patients was mainly made on the ground of clinical diagnosis.

The study showed also that there is no significant difference in the occurrence abnormal ECG in patients who reported to have history of status epilepticus. While the study done in USA shows significant correlation of status epilepticus with occurrence of abnormal ECG [48]. This discrepancy can be explained by the fact that later study was done prospectively along different time-frames.

5.6 LIMITATION OF THE STUDY

This research has its own limitation. Recall bias by the patients about their clinical information. Some patients could not remember the number of seizures that have had in the past. Lack of medical records regarding clinical information like status epilepticus and EEG data were also were also the limitation of the study Furthermore the diagnosis of epilepsy was made mainly based on clinical grounds without the use of EEG.

CHAPTER SIX: CONCLUSION AND RECOMMENDATION

7.1 CONCLUSION

The study showed that significant number of epilepsy patients have clinically important ECG abnormalities. The most common clinically relevant type of ECG abnormality detected was early repolarization pattern (ERP) followed by sinus bradycardia, RAD. Male sex was significantly associated with occurrence of ECG abnormalities. Twenty two patients were found to have ECG marker of SCD.

7.2 RECOMMENDATION

ECG abnormalities were common among adult patients with epilepsy at JUMC. ECG markers of increased risk of SCD were also found to be quite common among epilepsy patients. Early identification of such ECG abnormality can identify patients at high risk of SCD. Hence the study recommends routine use ECG to be utilized as part of chronic follow up care for epilepsy patients at JUMC follow up clinic.

Although our findings are derived from hospital based study, and hence may not be representative of the general Ethiopian population; we believe that this finding will provide invaluable, alarming, information for the local hospital and policy makers at large regarding ECG abnormalities and associated factors in epilepsy patients in our country**.**

We recommend health institutions and health professionals to build their capacity in identifying and intervening clinically significant arrhythmias in epilepsy patients. Physicians and other health professionals should be trained on risk factor for arrhythmia occurrence in epilepsy patients

Finally we strongly recommend that large prospective studies in this country is needed to improve precisions of these preliminary data to develop strategies that aim at early detection of Abnormal ECG in epilepsy patients and preventive strategies of SCD and SUDEP.

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DATA COLLECTION CHECKLIST

Patient's MRN Code

PART

SOCIODEMOGRAPHICINFORMATION

OF THE PATIENT

QUESTIONS	RESPONSE
Age in years	…….. years
1. Sex	A. Male ☐ B. Female ☐
2. Religion	A. Muslim ☐ B. Orthodox ☐ C. Protestant ☐ D. Others (specify_____
3. Ethinicity	A. Oromo ☐ B. Amhara ☐ C. Gurage ☐ D. D.Tigre ☐ E. Dawuro F. Yem ☐ G. Others (specify_____
4. Marital status	A. Single ☐ B. Married ☐ C. Divorced ☐

	D. Widowed ☐
5. Educational status	A. Illiterate B. Read and write ☐ C. Primary education ☐ D. Diploma ☐ E. Degree ☐ F. Post graduate ☐ G. Others (specify_____
6. Occupation	A. Governmental employee ☐ B. Merchant ☐ C. Student ☐ D. Daily laborer ☐ E. Farmer ☐ F. House Wife ☐ G. Others (Specify _____
7. Residence	A . Urban B.. Rural

PART II: INFORMATION ABOUT EPILEPSY

PHYSICAL EXAMINATION: VITAL SIGNS	FINDING
Blood Preassure	……mmgh
Pulse Rate	……..beat per minute
Respiratory rate	……....breaths per minute
Temprature	…….degree centigrade

PART II: CLNICAL CARACHTERSITCS

Question / parameter	

1. Age at the onset of epilepsy	…… years
2. Duration of epilepsy	……years
3. Type of epilepsy	A. Focal ☐ B. Generalized ☐ C. Unknown ☐
4. Are taking anti-epileptic medications?	A. Yes B. NO
5. If yes to the above question how long has it been since you start taking AEDs?	A. < 6 months B. 6 – 12 months C. 1- 2 years D. 2-5 years E. 5-10 years F. >10 years
6. Number and types of anti-epileptic drugs	A. One AED ☐ B. Two AEDs ☐ C. Three AEDs ☐ D. More than three AEDs ☐ E. Specific name of AEDs……
7. Seizure control /frequency of seizure per-month	A. No seizure in the past one year B. >5 times per year ☐ C. < 5 times per year ☐ D. 5-10 per month ☐ E. > per week ☐

	F. < 5 times per week ☐
8. Last episode of seizure before ECG was taken	A. < 6 hours ☐ B. 6-12 hours ☐ C. 12-24 hours ☐ D. >24 hours ☐
9. Other comorbid medical conditions	A. Heart Failure ☐ B. Stroke ☐ C. Hypertension ☐ D. Diabetes Mellitus ☐ E. Depression ☐ F. Other ------
10. If yes to above questions ? what specific drug use?	A. Antipsychotic ☐ B. Antidepressant ☐ C. Antihypertensive ☐ D. Antibiotic ☐ E. Other/specific drug……..
11. Etiology of epilepsy	A. Known ☐ B. Uknown ☐
12. If known what was the presumed etiology	A. Head trauma ☐ B. CNS infections ☐ C. Brain Tumor ☐ D. Other specific ☐ E. Metabolic ☐ F. Other ……..
13. Is there family history of epilepsy	A.YES ☐ B. NO ☐

14. History of status epilepticus	A. Yes ☐ B. No ☐