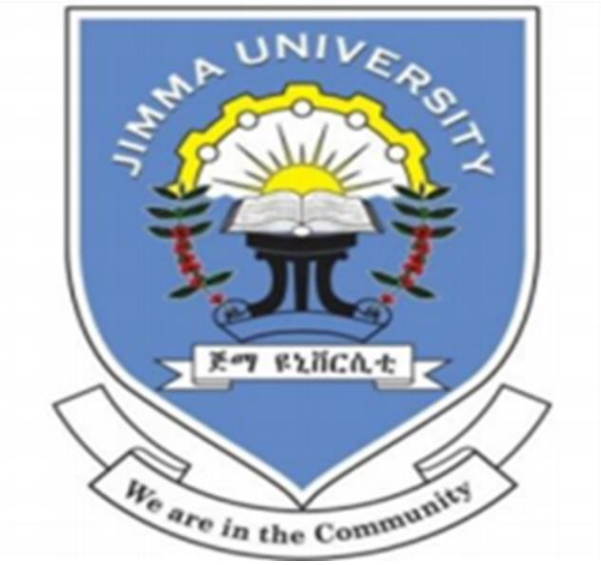

Analysis Determinants of Consciousness Level among Adult Stroke Patients: A Case Study of Jimma University Medical Center, Ethiopia

By: Tamiru Merera

A Research Thesis Submitted to Jimma University, College of Natural Sciences, Department of Statistics in Partial Fulfillment of the Requirements for the Degree of Master of Science in Biostatistics

Jimma, Ethiopia

November 2022

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Approval Sheet

I hereby certify that I have supervised, read, and evaluated this thesis titled "Analysis Determinants of Consciousness Level among Adult Stroke Patients: A Case Study of Jimma University Medical Center, Ethiopia " by Tamiru Merera prepared under my guidance. I recommend the thesis proposal be submitted for oral defense.

Geremew Muleta (Ass't Professor) ....…….

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Co - Advisor Signature Date

As the members of the board of examiners of MSc thesis open defense examination, we certify that we have read and evaluated the thesis and examined the candidate. Hence, we recommend that the thesis be accepted as it fulfills the requirements for the degree of Master of Science in Biostatistics

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Declaration

I declare that, this thesis is a result of my genuine work and all sources of materials used for writing it have been duly acknowledged. I have submitted this thesis to Jimma University in partial fulfillment for the Degree of Master of Science in Biostatistics. And also, I solemnly declare that I have not so far submitted this thesis to any other institution anywhere for that award of any academic degree, diploma or certificate.

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ABSTRACT

Background: A stroke happens when the blood flow to the brain is cut off or disrupted, which causes certain brain cells to die from a lack of oxygen. The most common type of stroke is ischemic stroke, also known as cerebral infarction. According to the American Heart Association, ischemic stroke accounts for 87 % of all strokes.

Objective: The primary purpose of this study is to identify the determinants of consciousness level among adult stroke patients at Jimma university medical center.

Methods: The study was carried out using a retrospective cohort study design and the secondary data was collected using the patient's chart under the follow-up. Samples of 310 stroke patients, measured repeatedly at least three times on each patient who are 18 years old or older those treated from January 2020 to December 2021. Data were analyzed by using R software version 4.0.5. The response variable Glasgow coma scale, which was measured longitudinally, was fitted using a linear mixed effect model.

Results: Among 310 stroke patients, Ischemic stroke 50.6% (n=157) whereas hemorrhagic stroke 49.4% (n=153). The average age at first visit was 55.72 ± 14.89SD, ranging from 19 to 91 years. Baseline age, Gender, stroke complication, histories of hypertension, history of diabetes, time and interaction time with baseline age were significance.

Conclusion: According to this study, women affected by stroke more than men because more women experience strokes throughout the course of their lives. The result shows that being hypertensive, older, having diabetic mellitus and having stroke complication, Age were significantly decrease the consciousness level of the stroke patients, implies as Age of a patients increase the level of consciousness decrease. Moreover, on average GCS measure increase in a linear pattern over time, implies as time increase the level of consciousness were increase. However being male and the time interactions with baseline age were significantly increases the consciousness level of the stroke.

Key Words: Stroke, Glasgow coma scale, Longitudinal Data Analysis; Linear Mixed Model.

Acknowledgement

First of all, I would like to thanks to Almighty God, who sustained me to this status and unlimited blessing. Also, my special gratitude goes to my advisor Mr. Geremew Muleta (Ass't Professor) and Co-Advisor Mr. Abiyot Negash (Ass't Professor) for their constructive comments and suggestions that contributed to the successful realization of this study. Again, i extend my sincere gratitude to all my staff for their unreserved knowledge sharing and cooperation

Contents

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List of Abbreviation

AIC : Akaike Information Criteria

BIC : Bayesian Information Criteria

CT : Computerized Tomography

DALY : Disability-Adjusted Life Year

DBP : Diastolic Blood Pressure

GBD : Global Burden Disease

GCS : Glasgow Coma Scale

GLM : Generalized Linear Model

HS : Hemorrhagic Stroke

IS : Ischemic Stroke

JUMC : Jimma University Medical Center

MRI : Magnetic Resonance Imaging

NIHSS : National Institutes of Health Stroke Scale

SBP : Systolic Blood Pressure

SSA : Sub Saharan Africa

IA : Transient Ischemic Attack

WHO : World Health Organization

CHAPTER ONE

1. INTRODUCTION

1.1. Background of the study

Stroke is a clinically defined condition marked by rapidly developing cerebral function symptoms or signs of focal failure with no obvious cause other than vascular origin, though the loss of function may also be global (applied to patients in a deep coma and those with subarachnoid hemorrhage) symptoms that last for more than 24 hours or result in death(1).

A stroke happens when the blood supply to the brain is cut off or burst, causing the death of some brain cells due to a lack of oxygen. Strokes are also a prominent cause of dementia and depression, Globally, 87% stroke is ischemic stroke most of time stroke-related deaths and disability-adjusted life years occur in low- and middle-income countries (2)**.** The most common type of stroke is ischemic stroke, also known as cerebral infarction. According to the American Heart Association, ischemic stroke accounts for 87 % of all strokes (3).

Infarcts occur when there is insufficient or interrupted blood flow to a part of the brain, usually due to a blockage of an artery, and hemorrhagic stroke is another type of stroke. The primary pathology is a bleeding region that causes direct brain tissue injury. These account for 10–15% of all strokes and have significantly higher morbidity and mortality rates than ischemic strokes(3). Unilateral or bilateral motor or sensory abnormalities, speech problems, altered mentation, headache, and vertigo are all common symptoms of a stroke. Stroke is diagnosed clinically, with a CT scan or MRI utilized to confirm the diagnosis and determine the kind of stroke. The treatment for a stroke is based on the type of stroke that has been identified, but general supportive measures such as airway management, coma care, catheterization, and selective provision of anti-platelets, anticoagulants, and thrombolytic therapy using intravenous recombinant tissue plasminogen activator are often used. In Ethiopians there no access to thrombolytic treatment(4).

Modifiable and non-modifiable stroke risk factors are the two types. Age, gender, and race (ethnicity) are non-modifiable risk factors for both ischemic and hemorrhagic stroke, but hypertension, smoking, diet, and physical inactivity are modifiable risk factors (5).

According to the Global Burden of Disease (GBD) study, over 11 million ischemic strokes occurred worldwide, with 63 percent occurring in low- and middle-income countries. In addition, about 3 million people died as a result of ischemic stroke, and around 13% of strokes are hemorrhagic. There were roughly 5.3 million hemorrhagic stroke occurrences, with about 80% of them occurring in low- and middle-income countries. Hemorrhagic stroke claimed the lives of about three million people (6).

In 2019, there were 12.2 million stroke event cases, 143 million DALYs due to stroke, and 6.55 million) stroke fatalities. The number of stroke that occurred increased by 70% from 1990 to 2019. The annual number of strokes and deaths due to stroke climbed by 43 percent and DALYs due to stroke increased by 32 percent, as did the yearly number of strokes and deaths due to stroke (6).Globally, it is ranked as the second leading cause of death with annual mortality rate of 5.5 million, and it is now the leading cause of physical disability in peoples aged 65 years and above in Developing countries have a higher burden of non-communicable diseases than the rest of the world and More-than two -third (70%) of strokes occur in low- and middle-income(6).

Strokes affect fifteen million people globally each year, according to the World Health Organization. Five million of these people were died, while another five million were permanently crippled. Excessive blood pressure is responsible for more than 12.7 million strokes worldwide. Nearly 650,000 people die from stroke every year in Europe. (7).

According to Global Burden of Disease Report, worldwide, 5.5 million deaths and 132 million are left permanently disabled related to stroke. In the same year in Asia 41.2%,and in Australia 14.9% of the stroke admission were died(8).

In Ethiopia, the overall in-hospital death rate for stroke was 18%. Stroke mortality rates in the Southern Nation's Nationalities and Peoples (SNNPR) and Tigray region were 19.6% and 15.1 percent, respectively, according to hospital-based studies (6). Stroke is becoming more common in Ethiopia, accounting for 7.5 percent to 19.3 percent of hospital admissions (9) and roughly 11% to 42.8 % deaths between 2014 and 2019.

There are clinical risk factors which lead to stroke. This is hypertension, DM heart failure, valvular heart disease coronary heart disease and atrial fibrillation. People with high levels of bad cholesterol /low density lipoprotein (LDL)/ and low levels of good cholesterol/high density lipoprotein (HDL)/have a greater risk of stroke. Foods that have a lot of saturated fats also have a lot of calories and can contribute to obesity that increases risk of getting stroke(10).

Most scholars recommend, 30-40 minutes exercise per day, to maintain a healthy weight and prevent obesity. Exercise and healthy diet are crucial for better heart & brain function. Heart disease and stroke share several equivalent risk factors, including hypertension, diabetes, and high bad cholesterol etc. Controlling these risk factors can result healthy brain and heart (11).

Diseases of the heart can lead to stroke through various mechanisms. Cardio embolic stroke is caused by clotted blood when it travels from the heart into the brain. Naturally circulatory system is supposed to prevent the formation of blood clots by keeping blood cells moving. When blood sits around, for instance atrial fibrillation, it tends to clot (12).

In Jimma A total of 116 eligible stroke patients were recruited during the study period. The mean age of the patients was 55.1 ± 14.0 years and males comprised 62.9%. According to world health organization (WHO) criteria of stroke diagnosis, 51.7% of patients had ischemic while 48.3% had hemorrhagic stroke. The most common risk factor identified was hypertension (75.9%) followed by family history (33.6%), alcohol intake (22.4%), smoking (17.2%) and heart failure (17.2%). The most common clinical presentation was headache complained by 75.0% of the patients followed by aphasia 60.3% and hemiparesis 53.4%. Atrial fibrillation was the independent predictor of hemorrhagic stroke (AOR: 0.08, 95% CI: 0.01–0.68)(13).

Thus, this study aims to identify Determinants of Consciousness Level among Adult Stroke Patients treated at JUMC using longitudinal data analysis.

1.2. Statement of the Problem

Stroke is a leading cause of death, disability, and sickness in both developing and developed countries, and it is a serious public health concern worldwide. Despite advancements in stroke research and treatment, as well as overall reductions in stroke mortality, stroke remains the third leading cause of death, trailing only heart disease and cancer, and the second leading cause of cardiovascular deaths, trailing only ischemic heart disease, with an annual incidence of about 15 million cases (14). According to research, in the United States, a stroke happens every 40 seconds on average, and at least one person dies from a stroke every four minutes (15).

According to WHO report, about 17.3 million people died of cardiovascular diseases representing 31% of all global deaths, from which stroke accounts for 6.7 million deaths. Among them four out of five deaths occurred in the low and middle income countries with men and women being equally affected (16).

According to the most recent GBD estimate, there is a continued shift away from communicable diseases, nutritional, and maternal causes and toward non-communicable diseases such as stroke (17). Chronic non communicable diseases account for 63 percent of all deaths.(9). The impact is more likely to be caused by the world's population growing and aging. Stroke accounts for roughly 3-4 percent of overall health-care spending in Western countries. In the United States, the average lifetime cost of a stroke, including inpatient treatment, follow-up care, and rehabilitation, is projected to be 140,048 dollars(17).

Stroke has a significant influence on disability and the loss of quality adjusted life years. It has a higher mortality rate in Sub-Saharan Africa, which accounts for 85 percent of all stroke-related deaths worldwide (10). Another rising impediment to socioeconomic development, particularly in developing nations like Ethiopia, is the invisible chronic disease burden epidemic (9). Even if the prevalence of stroke is substantially increasing in Ethiopia as well as in study area and also even if there are many studies conducted for stroke disease by separate analysis, as far as the author’s knowledge is concerned, the characteristic of a longitudinal study is that an individual is measured repeatedly through time. And in which a single outcome is measured repeatedly over time. However, In Ethiopia, there is a wide knowledge gap regarding stroke (18).

Even though the exact emergency burden of stroke in Ethiopia is not known, it has been estimated to be increasing and stroke accounts for 2.5% of all hospital admissions and 13.7% of medical admissions (19).

However, in Jimma although, admission to the hospitals due to stroke is increased over a time there is no such kind of enough research done on the cases of factors that suggested being associated with stroke. This in turn affects the quality of patient care. Even though, similar study on stroke were conducted in other parts of the world and Ethiopia, Most of the studies conducted on a stroke were done on Multivariable logistic regression (13) .

However, the stroke patients have follow-up starting from diagnosis date to event at every hospital. The characteristic of a longitudinal study is that an individual is measured repeatedly through time. And in which a single outcome is measured repeatedly over time .Due to the above gab there is scarce of a study conducted on linear mixed effect model Models fitted to longitudinal or repeated data involve the estimate of the covariance parameters to capture this correlation so, linear mixed effect model is the preferable model for follow-up data (longitudinal data). Therefore, this study aimed to identify Determinants of Consciousness Level among Adult Stroke Patients at JUMC using longitudinal data analysis.

Research Questions:

1. What are the determinants that are associated with consciousness level of adult stroke patients under treatment?

2. What is the rate of change of consciousness level of profile experienced adult stroke patients over time?

3. Which progressions of consciousness level stroke are high among predictor (explanatory) variables?

1.3. Objectives of the study

1.3.1 .General objective

The primary purpose of this study is to identify the determinants of consciousness level among adult stroke patients at Jimma university medical center from January 2020-December 2021.

1.3.2. Specific objective

1. To identify risk factors associated with consciousness level among adult stroke patients.
2. To estimate the rate change of consciousness level among stroke patients over time.
3. To compare the progression of Glasgow coma scale among predictor (explanatory) variables.

1.4. Significance of the Study

- ✓ The findings of this study will expected to give some knowledge about the determinants or risk factors that associated with consciousness level among adult stroke patients.
- ✓ These studies will providing information to government and healthcare bodies to make enabling environment for the intervention to reduce adult stroke patients.
- ✓ This study will expected to be helpful in identifying the most important covariates that have a significant impact on risk factors that associated with adult stroke patients .
- ✓ Moreover, the result of this study may be used as a source of information for other researchers in the future.

1.5. Scope of the study

The study was conducted in Jimma University Medical Center on identifying Determinants of Consciousness Level among Adult Stroke Patients by using the following variables; Age, systolic and diastolic blood pressure, gender, place of residence, history of hypertension, history of diabetes, history of heart disease, history of stroke complications, type of stroke ,history of HIV/AIDS and Time.

1.6. Limitation of the study

This thesis is not done without limitation. Repeated (longitudinally) measured data were not extracted well and it is very limited to specific area to obtain, in spite of this, it is preferred to extract data from medical cards of those already visited and registered at the respective hospital. There are many prognostic factors of stroke patients, such as; alcohol use, smoking status, body mass index, level of education, marital status, exercise and other. In this thesis, it is limited only to the above covariates. This is because all the necessary variables were not recorded on the patient's card, except those covariates.

1.7. Organization of the Research

Introduction**,** background of the study,statement of the problem, objectives of the study, literature review, methodology, study area, study design, study population and study period, data collection procedure and source of data, study variables, methods of data analysis , linear mixed effect model ,estimation of fixed effects, model selection, model checking technique , results and discussion and chapter five conclusion and recommendation.

CHAPTER TWO

2. LITERATURE REVIEW

2.1. Magnitude of stroke

According to a retrospective cohort conducted in Netherland Among 747 patient During follow-up, more than half of the patients 465 (62%) are died (20).another study conducted with the same design in Chang Gung on 1416 patient among this 805 hemorrhagic stroke and 611 ischemic stroke The in-hospital mortality rates of ischemic and hemorrhagic strokes were 15.9 and 20.4 %, respectively (21).

In Study conducted in Azerbaijan a total of 1036 stroke patients Among this 228 patients (22%) died within 30 days of after stroke occurrence (22). another study conducted with the same study design in Nigeria among 120 patients included. 74(61.7%) males and 46(38.3%) females 42 died at the end of study. from the death 32 (76.1%) died within the first seven days. Eight more patients died by the end of 30 days The last two died by the end of the three months of observation (23).

Data from national statistic from United Kingdome reveals that alcohol use12.8%, active Smoking 20%, past smokers 66%, alcohol, and illegal drug use 62%, diabetes mellitus 5%, high cholesterol use 21%, Illegal drug use 19.8% were factors associated with presence of stroke(24). According to the study conducted in Sweden the prevalence of stroke was 7% with a significant association of age, 65-80years (4.7%), >80 years (11.6%) and Sex; male 8.4% and female 5.7% (12).

According to the study conducted in South Brazile, the prevalence of stroke was 8.4% with a significant association of comorbidities like hypertension (29.8%), diabetes melitus (9.1%), age between 40-59years (39%)and 60-79years (16.8%), marital status widowed (7.6%),hypertension history from father 28.4% and Mother 45.6%, being male sex 44.1% and female 55.9% and smoking 27.4%(25).

Another study conducted in Ghana showed that 79.8% were women with 77.6% had hypertension, 18.4% had diabetes and hypertension, and 20 (4.0%) had just diabetes

(10).Furthermore, more effective treatment of childhood diseases will likely increase the proportion of elderly people in these countries, further increasing the burden of chronic disease. A large hospital based study in Tanzania estimated the incidence of stroke to be between 108-316 per 100,000 with significant differences between rural and urban populations (26).

Information concerning the community incidence of stroke is scarce with only one large study demonstrating a significantly lower incidence of stroke than hospital based studies (27).Reliable information on stroke in sub-Saharan Africa (SSA) is therefore poor and it is difficult to accurately estimate stroke incidence in its population. Nevertheless, the aforementioned studies demonstrate a steady, yet substantial increase in the burden of stroke, hence necessitating further research and implementation of appropriate prevention strategies. The rising incidence of stroke and stroke associated morbidity is especially problematic in SSA. Financial constraints and delayed presentation contribute to a high case fatality rate (28).

Multiple studies have identified hypertension as the leading risk factor for stroke in SSAs (26). with a Nigerian study demonstrating >80% prevalence of hypertension in stroke patients (29). Sub-Saharan populations appear to be more at-risk of developing hypertension and subsequent stroke. Current literature demonstrates higher mean systolic and diastolic blood pressures (BP) in people of African descent in comparison with their Caucasian counterparts (30). Study conducted at Tikur Anbesa specialized hospital shows that Stroke related complications were detected in 71.8% of the study participants and the most frequent complication was aspiration pneumonia which occurred in 33.8% but the other miscellaneous complications included were sepsis, hypokalemia exposure keratitis were detected in 25% of stroke patients which was common in patients with severe neurologic deficit as measured by Glasgow coma scale (GCS) and old age. Besides, GCS < 12 and age > 40 years were both significantly associated with developments of complications after stroke and a total of 23% patients died during their in-patient stay(31).

A study done on Luxemburg noted that 35.5% of study participants mentioned paralysis or weakness as a warning symptoms of stroke followed by speech disorder 32.1%, facial nerve palsy 15.7%, vertigo 15.2%, vision disorder 15.0%, loss of consciousness 14.1%, headache 12.9%, disorientation 11.2%, nausea/vomiting 9.1%, pain 5.5%, memory loss 5.2%, sensory symptoms 5.8%, death 1.9% and only 1.4% of respondents mentioned double vision as warning

sign of stroke whereas 10.2% of respondents didn't knew any warning symptoms of stroke at all (32). A study of diabetes patients in a primary care and diabetes practice center in Germany and Turkey found that 48.5 percent of respondents cited motor symptoms as a warning sign of stroke, followed by speech difficulty 36.6 percent, general symptoms 27.6 percent, vision 11.2 percent, sensory 6 percent, cranial nerve 24.6 percent, and coma 8.2 percent (33)Speech trouble (92.6 percent) was the most common warning symptom stated by respondents in a research done in Central Pennsylvania, followed by droopy face (88.3 percent), arm weakness (82.2 percent), and loss of balance (82.2 percent). Regarding distractors, neck pain (34.4%) and chest pain (33.1%) were commonly misidentified warning symptoms whereas back pain (16.6%) was the least misidentified warning symptom of stroke among respondents (34).

A study done on Cameroon revealed that the main warning signs and symptoms stated by respondents were speech disturbances (98.3%) followed by numbness or paralysis of one part of the body (98%), facial deformity (97.8%), sudden visual disturbance (91.2%) and headache (85.9%) (35)A cross sectional study done on Africa, Nigeria showed that from 239 respondents, 208 (87.0%) had good knowledge of the signs or symptoms of stroke. The warning symptoms commonly known by study participants were sudden and severe headache (86.2%), weakness on one side of the body (85.3%) and difficulty in speech (83.3%). Less than half of those surveyed (41.0%) recognized sudden loss of vision as a warning symptom of stroke and only 30.5% of participants knew reduced sensation in the body and sudden weakness all over the body (38.1%) weren't warning symptoms of stroke(36) .

A study done on Bahir Dar, Ethiopia revealed that around 77.3% of respondents did not recognize any warning symptoms of stroke. On the other hand, 14.4% of them recognized 5 and more warning symptoms, 5.4% recognized 4 warning symptoms and 0.7% recognized 3 warning symptoms. The most widely recognized warning symptoms of stroke by respondents were (35.9%) paralysis or weakness on one side of the body and (16.2%) severe headache (14).

2.2 .Knowledge of Stroke Risk Factors

A study done on Luxemburg stated that, among 420 in and outpatients in neurology department 40.2% of study participants mentioned smoking as stroke risk factor followed by arterial hypertension 32.4%, alcohol 32.1%, nutrition 27.6%, cholesterol 26.4%, stress 22.6%, lack of physical exercise 19.3%, overweight 14.3%, hyperlipidemia 13.1%, peripheral arteriopathy 7.9%, hereditary factors 7.1%, diabetes mellitus 6.2%, poor circulation 4.3% and age 3.8%. While 10.5% of respondents didn't knew any risk factors of stroke at all(32).

Similarly, According to a survey examining African Americans' awareness of stroke risk factors, the majority of respondents had no idea how lifestyle factors like lack of physical activity, excessive alcohol use, diabetes, smoking, and high cholesterol affect the risk of stroke. According to research, changing such stroke risk factors can cut the risk of stroke by 80% (36).

A study done among diabetes patients from Germany and Turkey noted that 35.8% of respondents recalled hypertension as a risk factor of stroke followed by smoking 35.1%, hyperlipidemia 6.7%, diabetes mellitus 17.9%, alcohol 15.7% and only 3.7% of respondents stated heart disease as a risk factor of stroke. Their study discovered the lack of knowledge of stroke risk factors among diabetics in natives and migrants in Germany. They also noted that, patients younger than 61 years had better stroke knowledge than those older (36).

A study conducted in Cameroon noted that the main risk factors mentioned by study participants were hypertension (98.5%) followed by overweight (97.8%), lack of physical activity (97.7%), stress (95.1%), family history of stroke (87.4%), unhealthy diet (85.5%), alcoholism (64.2%), smoking (60.6%), and hypercholesterolemia (44.4%) (19). Another study done on hypertensive and diabetic patients revealed that, more than half of respondents (86.6%) had good knowledge towards stroke risk factors. The most frequently reported stroke risk factors were hypertension (92.0%), too much fat consumption (85.7%), overweight (84.9%) and not exercising regularly (80.8%). Less than half of study participants recognized aging (42.3%) and use of oral contraceptives (42.3%) as risk factors of stroke (16).

According to the study done on Bahir Dar, Ethiopia, the most common risk factor of stroke mentioned by respondents were physical inactivity (21.6%) followed by obesity (20.1%) and drinking alcohol (18.7%). Majority (77%) of survey participants could not recognize any stroke risk factors; 14% recognized 5 risk factors; 3.6% recognized 4 risk factors; whereas only 1.8% recognized 3 risk factors of stroke (14).

Linear mixed-effects models are highly attractive due to their ability to handle missing and unbalanced data reasonably well. Stroke is one of the most common non-communicable illness causes of morbidity and mortality. In Sub-Saharan Africa including Ethiopia It's occurrence has been steadily growing. In this domain, mortality is also greater than in developed nations. Thus, this study aims is to identify Determinants of Consciousness Level among Adult Stroke Patients treated at JUMC using longitudinal data analysis

CHAPTER THREE

3. METHODOLOGY

3.1. Study area

The study was conducted in Jimma University Medical Center (JUMC), Jimma, Ethiopia. Jimma is found in south western Ethiopia and 346 km far from Addis Ababa, capital city of Ethiopia. JUMC has endured time as one of the oldest public hospitals in Ethiopia. This hospital serves as a medical center for the catchment of Jimma city, 21 woreda and different surrounding areas.

3.2. Study Design

A retrospective cohort study design was carried out by retrieving relevant information from the medical records of stroke patients.

3.3. Study population and study Period

The target population of the study was all adult stroke patients with age ≥18 years at JUMC. The study period was patients who started treatment from January 2020 to December 2021.

3.4. Data collection procedure and Source of Data

Two years data (from January 2020-December 2021) total patients admitted to the Jimma university medical center with the diagnosis of stroke were taken .Since the total 310 study subjects were taken, there was no sampling method used. The data was collected by using secondary data collection process by reviewing the patient's chart and follow-up cards on a stroke patient. The longitudinal data was extracted by using two nurses from the patient's chart which contains socio-demographic and clinical information of all adult stroke patients under the treatment. Since the longitudinal response variable was continuous linear mixed effect model is must be used. The data consists of 310 individuals with a minimum of four and maximum of fifteen GCS measurements (consciousness level of stroke) and other covariates were measured per individual of adult stroke patients. Patents‟ follow up time was one , two or three months gab according to the order of the doctor and the data were recorded on patients‟ medical follow up card by assigning an identification number per individual by health workers in the chronic follow up clinic, which helps to find the patients profile easily during his/her next visit time.

3.5 .Eligibility criteria

3.5.1. Inclusion criteria

All patients admitted to the selected hospitals during the study period who were fulfill the World Health organization's case definition of stroke and who had a CT scan report of stroke and those patients age ≥18 years old and who have followed at least three visits from January 2020 to December 2021. Out of the total 400 stroke patients were 310 included in the study.

3.5.2. Exclusion criteria

Those patients <18 years old and who did not fulfill the definition of stroke and patient records with incomplete information mainly with no diagnosis and who have followed less than three visits, out of the total 400 stroke patients were 90 excluded from the study.

3. 6.Operational definition

Stroke: happens when brain attack and blood flow to your brain is stopped. It is an emergency situation according to WHO criteria it is clinically defined as rapidly developing clinical evidence of localized or global impairment of brain function, lasting 24 hours or longer or resulting to death, with no evident cause other than vascular origin.

Ischemic Stroke: it occurs when the artery that provides oxygen-rich blood to the brain becomes blocked and caused by blood clots.

Hemorrhagic Stroke: It occurs when a blood artery weakens and ruptures, causing bleeding into the surrounding brain tissues.

3.7. Ethical Considerations

The ethical clearance and permission was obtained from Research Ethical Review Board of college of Natural Sciences, Jimma University before starting data collection. An ethical clearance letter from Jimma University was given to Manager of the Jimma University Medical Center and a permission letter was obtained. The researcher was collect (1) patient history from record (hard/electronic sources) only by a trained health professional assigned by the concerned institute, (2) all data collected (both secondary and primary) was treated with maximum confidentiality, the identity of the respondents/patients was never be exposed to anyone at any time by any means, (3) the information/data was never be used for any other purpose than for the scientific goal and was never be transferred to any third party with identity of the respondents/patents.

3.8. Study Variables

3.8.1. Response Variables

The continuous variable for this study is; Glasgow Coma Scale (GCS**).** Glasgow coma scale (GCS) : - is Helps to measure level of stroke consciousness (severity).Level of consciousness is a term used to describe a person's awareness and understanding of what is happening in his or her surroundings. GCS measures the following functions; eye opening (E=4), verbal response (V=5), Motor (M=6).so the sum of E+V+M =15, the maximum values of Glasgow coma scale is 15, whereas the minimum values of Glasgow coma scale were 3. Glasgow coma scale (GCS) increase implies that there is consciousness level of stroke (Good). Glasgow coma scale (GCS) decrease implies that there is unconsciousness level of stroke (bad).

3.8.2. Explanatory Variable

According to different literature review the following variables is considered as explanatory variables for this study and Covariates associated with adult stroke patients comprise baseline socio-demographic and clinical variables were presented in Table 3.1

Table 3.1: Predictor variables and coding

Variable	Values of the variables and their code	Type
Age	Years(baseline)	Continuous
Systolic blood pressure	mm Hg(baseline)	Continuous
Diastolic blood pressure	mm Hg(baseline)	Continuous
Time	in months (baseline)	Continuous
Gender	[Female = 0 (reference), Male = 1]	Categorical
Residence	[Rural = 0 (reference), Urban=1]	Categorical
Types of stroke	[Hemorrhagic=0(reference),Ischemic=1]	Categorical
History of hypertension	[No = 0(reference), Yes = 1]	Categorical
History of diabetes	[No = 0(reference), Yes = 1]	Categorical
History of heart disease	[No = 0(reference), Yes = 1]	Categorical
Stroke Complication	[Yes = 0(reference), No= 1]	Categorical
History of HIV/AIDS	[No = 0(reference), Yes = 1]	Categorical

3.9. Statistical Methods of Data Analysis

The Linear Mixed Model (LMM) has become the most commonly used tool for analyzing continuous repeated measures data.

One of the major objectives of statistical analysis is to address variations in the data. For longitudinal data, there are two sources of variations: within-subject variation; the variation in the measurements within each subject, and between-subject variation; the variation in the data between different subjects. The linear mixed-effects model is a parametric linear model for longitudinal or repeated measures data that quantifies the relationships between a continuous dependent variable and various predictor variables. The term repeated measures is used to describe the longitudinal data. Predictors of Consciousness Level within-subject variation allows studying changes over time, while Predictors of Consciousness Level between-subject variation allows understanding differences between subjects.

In this study, longitudinal measures on the GCS and various socioeconomic variables and clinical factors of stroke were considered and analyzed using descriptive statistics with a thoughtful and thorough of the data. This includes exploratory data analysis to use an appropriate statistical model to the data. Hence, individual profile plot, mean profile plot, the normal Q-Q plot were performed. We used R software version 4.0.5 to analyze the data, with a 5% level of significance.

In longitudinal data, the subjects (an individual) are measured repeatedly through time this requires special statistical methods because the set of observations on one subject tends to be inter-correlated. This correlation must be taken into account to draw valid scientific inferences. Models fitted for longitudinal measures data involve the estimation of covariance (correlation) parameters to capture this correlation between subjects (36). The linear mixed-effects model (LMM) is a parametric linear model for longitudinal or repeated measures data that quantifies the relationships between a continuous dependent variable and various predictor variables. It is extending from the classical linear regression model that takes into account both fixed effect and random effect. The random effect contains a subject-specific effect and the fixed effect contains the set of predictors that are fixed across the subjects or the same for all subjects. In LMM the fixed

effect parameters describe the relationships of the predictors to the dependent variable for an entire population; random effects are specific to subjects within a population. Consequently, random effects are directly used in modeling the random variation in the dependent variable at different levels of the data (37).

3.9.1. Exploratory Data Analysis

The first step in any model building process is exploratory data analysis. Data exploration is a very helpful tool in the selection of appropriate models to visualize the patterns of data relative to research interests. Analyses of longitudinal data compare profiles over time and, indeed, time might be viewed as the primary systematic effect to be investigated. The aim of this process is to understand the data structure and determine the relevant modeling approaches suitable for it.

3.9.1.2 .Exploring the Individual Profile

To explore the individual profile, plot of the response with time is used to show whether there is a noticeable pattern common to most subjects. These individual profiles can also provide some information on within and between subject variability. Plotting observed profiles over time helps to identify general trends within subjects and may detect change over time that provides information about the variability at given times.

3.9.1.3. Exploring the Mean Structure

Examining the data for clues about the likely nature of the mean structure, to see how the mean profile changes over time, is essential for specifying the functional form of the mean response of the model. So as to understand the possible relationships among means over time, for balanced data, graphical inspection can be used by connecting the average values computed at each time point separately. If the data is not balanced and unequally spaced interval loess smoothing can be used instead. In this study the data is unbalanced and also unequally spaced interval loess smoothing technique is used instead of mean structure over time. This will give idea as to how the mean profile evolves over time. The results of this exploration will be useful in order to choose a fixed-effects structure for the linear mixed model.

3.9.1.4. Exploring the Random Effects

The first step in the model building process for a linear mixed-effects model, after the functional form of the model has been decided, is choosing which parameters in the model, if any, should have a random-effect component included to account for between group variations. The **lmList** function and the methods associated with it are useful for this. The main purpose of this exploring the random effects analysis is to give an indication of what random effect structure to use in the model. We must decide which random effects to include in a model for the data, and what covariance structure these random effects should have.

3.9.1.5. Exploring the Correlation Structure

It helps to describe how measurements within an individual correlate. The correlation structures studied through the correlation matrix, or a scatter plot matrix.

3.9.1.6. Exploring the variance structure

In exploring the variability of the Observed data we analyze the variance at each time point for the variables and check their Variability..

3.9.2. Linear Mixed Effect Model

A commonly used mixed effects linear model for continuous response variables was proposed by (38).The name mixed model indicates that the model contains both the fixed or the mean model component and the random component and variable effects are either fixed or random depending on how the levels of the variables that appear in the study are selected (38). Through random effects models, we can make inferences over a wider population in linear mixed models than possible with general linear models. The first step in the model building process for a linear mixed-effects model, after the functional form of the model has been decided, is choosing which parameters in the model, if any, should have a random-effect component included to account for between-group variation. Unlike general linear model family, linear mixed models are models that handle data where observations are not independent. Many longitudinal studies are designed to investigate change over time in a characteristic which is measured repeatedly for each patient (38). The advantage of a longitudinal study is its effectiveness for studying change. Investigators gather repeated measures or longitudinal data in

order to study change in a response variable over time as well as to relate these changes in explanatory variables over time (39).

The linear mixed model has become the most commonly used tool for analyzing continuous repeated measures data from a sample of individuals and the term `individual' will have different interpretation or meaning for different areas of application. Next we will explain how measurements may be taken repeatedly on the same unit. The general linear mixed model extends the general linear model by the addition of random effect parameters and by allowing a more flexible specification of the covariance matrix of the random errors. The subject-specific regression coefficients reflect how the response evolves over time for each subject. These subject-specific models can be very flexible, but in practice polynomials involving time will often suffice. However, extensions of this flexibility, such as fractional polynomial models or extended spline functions, can be considered as well (40).

Random effects contribute linearly to the response, the model is called linear mixed-effects model. The linear mixed model is defined as:

$$Y_i = Z_i(K_i\beta + b_i) + \varepsilon_i = Z_iK_i\beta + Z_ib_i + \varepsilon_i$$

where $Z_iK_i = X_i$ and the final model becomes

$$Y_i = X_i\beta + Z_ib_i + \varepsilon i$$

Where

- Y_i is the $N_i \times 1$ response vector for ith subject: $Y_i = (Y_i1, Y_i2, \ldots .. Y_iN)$
- Z_i is a $N_i \times q$ matrix of known covariates
- X_i is a $N_i \times p$ design matrix for the fixed effects
- β is a $p \times 1$ dimensional vector of subject specific regression coefficients
- b_i is $q \times 1$ dimensional vector of unknown random effects
- ε_i is $N_i \times 1$ error vector $\varepsilon_i \sim N(0, \Sigma_i)$, often $\Sigma_i = \sigma^2 I_{ni}$
- $b_i \sim N(0, G)$ i. e:- b_i has a q-variate normal density with mean vector 0 and a variance covariance matrix G

In this model, $Xi\beta$ is the mean response and $Zibi$ incorporates the random effects part.

Assumptions of Linear Mixed Effects Model: Before making inferences about a fitted mixed effects model, we should check whether the underlying distributional assumptions appear valid for the data or not. There are two basic distributional assumptions for the linear mixed effects model. I. $\varepsilon i \sim N(0, \sigma^2 I_{ni})$

The within-group errors are independent and identically normally distributed with mean zero and variance $\sigma^2 I_{ni}$ and they are independent of the random effects

II. $bi \sim N(0,G)$

The random effects are normally distributed, with mean zero and covariance matrix G (Not depending on the group) and are independent for different groups. The most useful of methods for assessing the validity of these assumptions were based on Q-Q plots of the random effects.

3.9.2.1. Estimation of Fixed Effects

Both the maximum likelihood (ML) and restricted maximum likelihood (REML) were used for estimation of the parameters in this study. The maximum likelihood estimation method finds the parameter estimates that are most likely to occur given the data. The parameter estimates are derived by maximizing the likelihood function, which is a mathematical expression that describes the probability of obtaining the data expressed as a function of the parameter estimates (41) .

3.9.2.2. Maximum Likelihood Estimation

The maximum likelihood estimation method finds the parameter estimates that are most likely to occur given the data. The parameter estimates are derived by maximizing the likelihood function, which is a mathematical expression that describes the probability of obtaining the data expressed as a function of the parameter estimates (40). Suppose a random sample of N observations is obtained from a linear mixed effect model as defined above, then the likelihood of the model parameters, given the vector of N observations, is defined as:

$$L=l(\beta, \theta, Y_i)= \prod_{i=1}^{N}\{2\pi^{-1/2} |V|^{-½} \exp(-\frac{1}{2}(Y_i - X_i\beta)' V^{-1}(Y_i - X_i\beta))\}$$

Where: - β is a vector of fixed-effects parameters and θ is a vector containing the variance parameters. Given its simplicity in comparison to the likelihood function, the log of the

likelihood function is generally used in practice. Its maximum value coincides with that of the likelihood function. The log-likelihood of the model parameters, is defined as

$$\text{Log L}=\text{l}(\beta, \theta, Y_i)= -\frac{\text{N}}{2}\log (2\pi) - \frac{1}{2}\log| V |- \frac{1}{2} (Y_i - X_i\beta)' \text{V}^{-1} (Y_i - X_i\beta)$$

$$=K - \frac{1}{2}\log |V |- \frac{1}{2} (Y_i - X_i\beta)' \text{V}^{-1} (Y_i - X_i\beta)$$

$$\text{Where} \quad \text{K}=\frac{N}{2}\log (2\pi) , \qquad \text{V}=\text{Z}_\text{i}\text{GZ}_\text{i}'+ \Sigma_i$$

Now the values in the model parameters which maximize the log-likelihood may be determined. Estimates of the parameters are found by maximizing the log-likelihood given in above equation with respect to β and θ. One such method that may be used to maximize the log-likelihood function is the maximum likelihood (ML) method. The ML method first maximizes the log likelihood with respect to the variance parameters, while treating the fixed-effects parameters, β,as constant. Upon determining the variance parameter estimates, the fixed-effects parameters are then determined by finding the values of β which maximize the log likelihood, while treating the variance parameters as constant. It is important to note, the maximum likelihood approach may produce variance parameters that are biased downwards since they are based on the assumption that the fixed-effects parameters are known (42).

Thus , $\frac{\partial \text{l}}{\partial \beta} = -\text{X}_\text{i}\text{V}^{-1}\text{X}_\text{i}\beta + \text{X}_\text{i}'\text{V}^{-1}\text{Y}_\text{i}$

Then, the MLE of $\hat{\beta}$ on combining all the information from all the N subjects equals

$$\hat{\beta}=(\sum_{i=1}^{N} \text{X}_\text{i}'\text{V}^{-1}\text{X}_\text{i})^{-1} \sum_{i=1}^{N} \text{X}_\text{i}'\text{V}^{-1}\text{Y}_\text{i}$$

3.9.2.3. Restricted Maximum Likelihood Estimation

This is another method that may be used to maximize the log-likelihood function. Sometimes this method is referred to as the restricted maximum likelihood method. It was developed in order to avoid biased variance component estimates that are produced by ordinary maximum likelihood estimation. This is because maximum likelihood estimates of variance components takes no account of the degrees of freedom used in estimating fixed effects. This means that ML estimates of variance component have a downwards bias which increases with the number of fixed effects in the model. For this approach, the fixed-effects parameters, β, are eliminated from

the log-likelihood equation, such that it will only be defined in terms of the variance parameters. Then, a likelihood function based on the full residuals, (Y_i-$X_i\hat{\beta}$). It may be noted that the full residuals are a linear combination of y and furthermore (Y_i-$X_i\hat{\beta}$) and $\hat{\beta}$ are independent (43). From these facts, the log-likelihood for β and the variance parameters, θ, may be express as a product of the likelihoods based on (Y_i-X_i $\hat{\beta}$) and $\hat{\beta}$

$$L(\theta, \beta; Y_i) = L(\theta; Y_i - X_i\beta) L(\beta; \hat{\beta}, \theta)$$

Thus, yields the REML, defined as

$$L(\theta; Y_i - X_i\hat{\beta}) = |X_i' V^{-1} X_i|^{-1/2} |V|^{-1/2} \exp\{ - \tfrac{1}{2}(Y_i - X_i\hat{\beta})' V^{-1}(Y_i - X_i\hat{\beta})\}$$

Therefore, the REML log-likelihood is defined as

$$\text{Log } L(\theta; Y_i - X_i\hat{\beta}) = K - \frac{1}{2}\{\log |V| - \log |X_i' V^{-1} X_i|^{-1} + (Y_i - X_i\hat{\beta})' V^{-1}(Y_i - X_i\hat{\beta})\}$$

Despite β appearing in the REML log-likelihood in the above equation, it is present only as a function of the variance parameters. As with the maximum likelihood method, the variance parameters are now estimated by maximizing the REML log-likelihood with regards to the variance parameters. Given the nature of the REML likelihood, and its treatment of the fixed effects as parameters, rather than as constants, the resulting variance parameter estimates are unbiased. In the same fashion of the maximum likelihood method, values of $\hat{\beta}$ are found by maximizing the REML log likelihood with regards to the fixed-effects parameters, while treating the variance parameters as fixed.

3.9.2.4. Covariance Structure

Covariance structures are just patterns in covariance matrices. A model for the covariance must be chosen based on some assumed model for the mean response. To reduce the number of parameters in the variance-covariance structure Σ, we can fit models with more parsimonious structures. Because it decreases the number of parameters, the covariance is frequently given a simplified form and can improve model convergence. There are a variety of covariance structures that cover a variety of assumptions regarding the relationships between replies from the same person. However, when the longitudinal response variable has an unbalanced or unequal space interval of time i.e., the correlation between responses is comparatively complex, or when the variance is heterogeneous ,an unstructured covariance structure is appropriate to get

efficient estimates relative to other covariance structures (44). Since in this study, the longitudinal response variable was measured at different times. It is also crucial to include a significant number of free parameters in the fitting process. Due to these assumptions, an unstructured covariance structure was assumed preferable.

3.9.2.5. Model selection

After getting the series of models that have been fitted for the actual data the next move are was to select the simplest model that best adapts to the data observed. Akaike information criteria (AIC), and Bayesian information criteria (BIC), and we use AIC or BIC for non-nested models.

Akaike information criteria (AIC)

The Akaike information criteria (AIC), originally introduced by Akaike(45), is popular model assessment criteria for model selection. AIC is defined by

$$AIC = -2\log(l_{max}) + 2k$$

Where $l_{max}$is the maximum value of the current model's likelihood function and k is the number of parameters. By this criterion, among all candidate models, the one with the smallest AIC value can be selected. In this study, we have used AIC for model selection and comparison of linear mixed-effect model.

Bayesian information criterion (BIC)

The Bayesian information criterion is another popular model assessment criterion for model selection. The BIC is given as follows:

$$BIC = -2\log(l_{max}) + k\log(n)$$

By contrasting the BIC score with the AIC score, it can be seen that the former puts more penalty on the number of parameters k in cases when log (n)>2. the BIC has consistency property in the sense that the probability of selecting the true model would approach 1when n increase and when the true model is among all candidates models under consideration, and AIC criterion has the asymptotic optimality property in the sense that it can asymptotically choose the best possible model. In this study, we have used BIC for model selection and comparison of linear mixed-effects model.

3.9.2.6. Model Checking Technique for Linear Mixed Model

For linear mixed effects models, the assumption of normality needs to be assessed by looking at residual errors. It is assumed that the random effects are normally distributed and uncorrelated with the error term. Residual plots can be used visually to check normality of these effects and to identify any outlying effect categories. Examining the plot of the standardized residuals versus fitted values by any covariates of interest can give a better feeling (46).The assumption of normality for the within-group error was assessed with the normal probability plot of the residuals by covariates. Similarly, Normality of the random effects is assessed using Normal Plot of each random effect. Normal plot of estimated random effects helps for checking marginal normality and to identify outliers.

CHAPTER FOUR

4. RESULTS AND DISCUSSION

4.1. Results

4.1. 1.Baseline Information and Descriptive Statistics

A total of 310 stroke patients with a minimum of four and maximum of fifteen measures of GCS. The mean average of GCS was 11.84 and other covariates per patient were included. The baseline characteristics and descriptive statistics of patients are displayed in tables 4.1 below. From the total number of participants involved in the study, the majority of the stroke patients, 67.7 %(n=210) were females. About 133 (42.9%) of stroke patients were living in rural. About 157(50.6%) of stroke patients were ischemic stroke. Of total participants in this study, more than half 172 (55.5 %) of them were diagnosed with diabetes mellitus. About 281(90.6%) stroke patients were diagnostic hypertension. About 236(76.1%) of stroke patients were had history of heart disease, All most 282(91.0%) of stroke patients were had stroke complication. the average age at first visit was 55.72±14.89SD, ranging from 19 to 91 years Table (4.1).

Table 4.1: Frequencies and Percentages for baseline categorical covariates

Variable	Categories	Number (%)
Gender	Female	210(67.7)
	Male	100(32.3)
Residence	Urban	177(57.1)
	Rural	133(42.9)
Type of stroke	Hemorrhage	153(49.4)
	Ischemic	157(50.6)
History of hypertension	Yes	281(90.6)
	No	29(9.4)
History of diabetic mellitus	No	138(44.5)
	Yes	172(55.5)
History of heart disease	No	74(23.9)

	Yes	236(76.1)
Stroke complication	Yes	282(91.0)
	No	28(9.0)
HIV/AIDS status	No	28(9.0)
	Yes	282(91.0)

4.1.2. Exploratory Analysis

Before developing a model, plots are crucial for visualizing the evolution of the Glasgow Coma Scale measurements over time. Various plots have been investigated to reveal the patterns pertinent to the scientific inquiry about the Glasgow coma scale progression of stroke patients.

4.1.3. Exploring Individual Profile plots of Glasgow coma scale over time

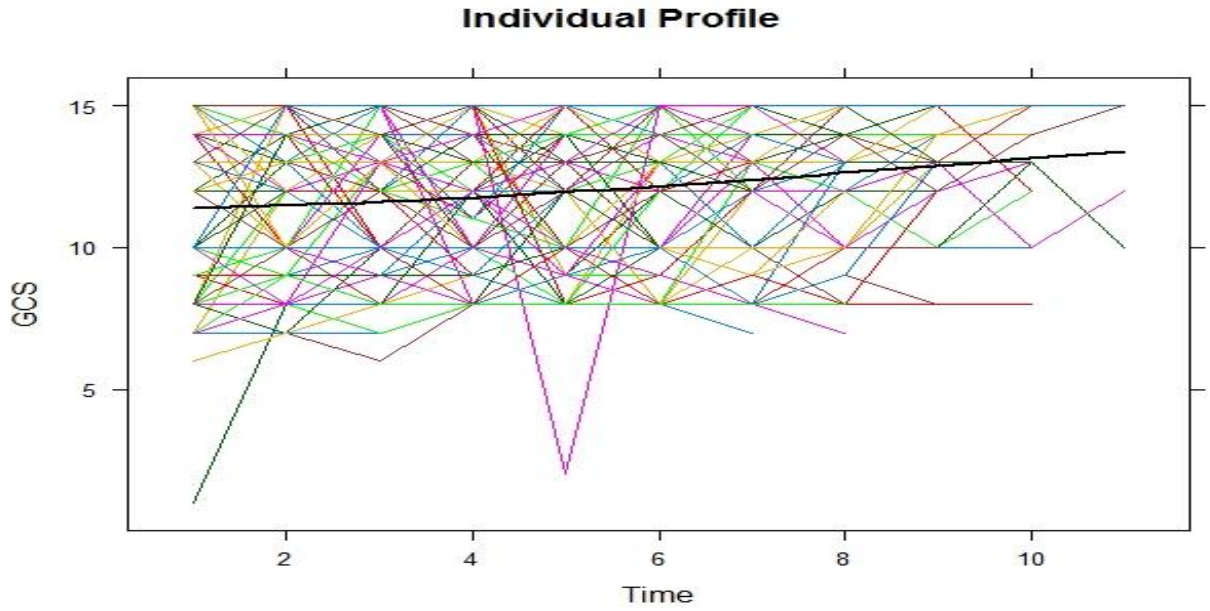

Figure 4.1: Individual profile plot of Glasgow Coma Scale

Figure 4.1 illustrates how the variability of the GCS amongst people appears to be larger at baseline and to be getting higher over time. Additionally, Also it shows variation in the GCS across and among participants, suggesting that the between and within subject specific variances cannot be disregarded

4.1.4. Mean profile Plots Glasgow Coma Scale Stroke patients

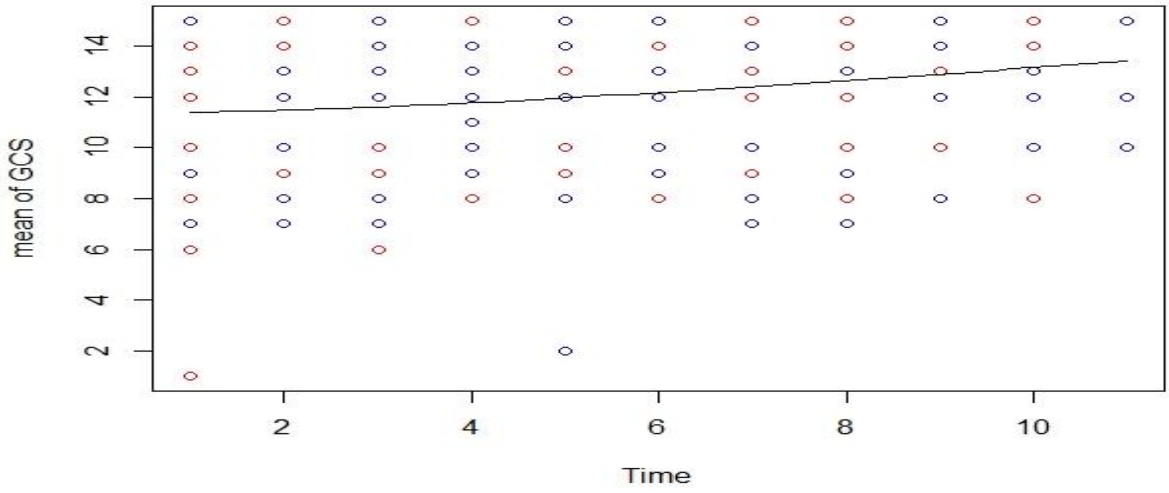

Figure 4.2 : Mean profile plot of GCS of stroke patients

The loess smooth curve in Figure 4.2 implies a linear link between the average profiles of GCS across time. It suggests that the GCS exhibits a rising trend over time. Additionally, it suggests that the linear temporal effects could be incorporated into the model as fixed effects

4.1.5. Exploring the Random Effects

The major goal of studying random effects is to provide guidance on what random effect structure should be utilized to create a linear mixed model of stroke patients' Glasgow coma scale. To explore, we create an interval plot for the estimated coefficients using the lmList estimation. The interval of scatter plots matrix in (Appendix) show that there are differences in the intercept and slope of the linear function. Therefore, to fit the linear mixed model for the Glasgow coma scale stroke patients' data, we need a random intercept and a linear slope random effect.

4.1.6. Exploring the variance structure over Glasgow coma scale

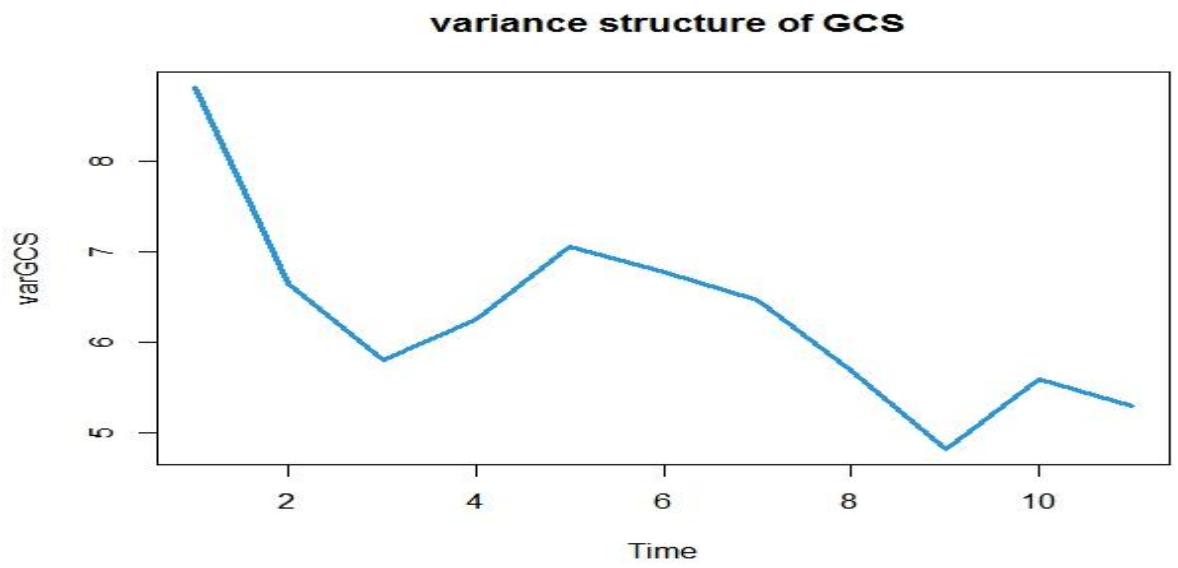

Figure 4.3: Over all variance structure of Glasgow coma scale stroke patient's data

According to the variance structure Figure 4.3 of stroke patients above, it appears that the observed variance is not constant over time; rather, the recorded values of variance drop up to 3 months of age and then increase after up to 5 and drop up to 9 again and increase up to 10 month and decrease.

4.1.7. Exploring the correlation structure

The correlation structure describes how measurements within a subject correlate. The correlation between GCS at each time points is given by plot matrix in (Appendix).

4.2. Linear Mixed Effects Model

The purpose of this section is to choose a series of fixed and random effects in order to fit a linear mixed model for the GCS.

To select the fixed effect components of the response variable, GCS, including all covariates and interaction terms with time without considering the corresponding different random effects

4.2.1. Selection of Fixed effects

We can see from the results in Table 1 (Appendix) that age, stroke type, blood pressure, stroke complications, history of hypertension, history of diabetes mellitus, and time were statistically significant factors, whereas gender, residence, history of heart disease, and HIV/AIDS were not. Ages with time, stroke type with time, and stroke complexity with time were statistically significant interaction effects, whereas the other interactions were insignificant. Thus, the insignificant terms should be removed from the model starting with the most insignificant one of which is the interaction term systolic blood pressure by time with p-value of 0.994. The model was then refitted after removing the interaction term systolic blood pressure by time and the AIC dropped from 9787.198 to 9785.198 indicating a better fit.

The model was fitted again and the interaction term gender by time was still insignificant. The next step is to remove the interaction term gender by time with the p-value of 0.927. The model was fitted again and the AIC dropped from 9785.198 to 9783.282. The next step is to remove the interaction term History of hypertension by time with the p-value of 0.729. The model was fitted again and the AIC dropped from 9783.282 to 9781.489. By following the same procedure the final fixed effect model for Glasgow Coma Scale is given by:

$$Y_i = \ 10.8 - 0.33\ Gen_i + \ 0.095\mathrm{HI}V\ + 0.29\ Hh_i + 0.18\ Hhd_i + 0.82\ T_{ij} - 0.005\ Age_i - 0.03\ Res_i + 0.10\ Type_{i_i} + 0.04\ Hd_i - 0.05 Hhd_i - 0.003 Dbp_i - 0.20 Scom_i.$$

Hence, in this study gender, HIV/AIDS status, History of hypertension, age, place of residence, type of stroke, history of diabetic mellitus, history of heart diseases, diastolic blood pressure, stroke complication, time and the interaction terms age by time, residence by time, type of stroke by time, history of diabetic mellitus by time, history of heart disease by time diastolic blood pressure by time stroke complication by time were used as fixed effects in the model for Glasgow Coma Scale.

4.2.2. Selection of Random Effects

In this section the aim is to select the random effect model of the rate of change of GCS measure over time including all potential covariates. In order to retain or remove the random effects from the model, it is better to fit the linear mixed effects model with different random effects. Thus, four different models with different random effects starting from a simple linear regression model (no random effects) have been explored. Table 4.3 shows summary measures; Akaki information criteria (AIC) and Bayesian information criteria for the models with different random effects. An appropriate random effect to the model was selected by using AIC value. The conclusion is consistent with the AIC and the BIC values for which smaller value is considered as better. That is, the AIC information criterion decreased from 9781.489 to 8115.913, which indicates that model with intercept and slope, was a better fitting model. Therefore, both AIC and the BIC criterion suggests including the quadratic time slopes as random effects does not improve the model fit. As a result, the random quadratic time slopes are not included in the subsequent analyses.

Table 4.2: Selection of Random Effects to be included in the Linear Mixed Effects Model for GCS.

No.	Random Effects Included	AIC	BIC
1.	No Random Effects	9781.489	9899.84
2.	Random Intercepts	8653.369	8777.143
3.	Random Intercepts and Linear Slopes	8115.913	8270.299
4.	Random Intercepts, Linear and Quadratic Slope	8135.191	88250.939

Source: Jimma University Medical center, Ethiopia; from January, 2020 to December, 2021

As shown in Table 2 (Appendix), type of stroke and interaction terms history of diabetic mellitus by time, stroke complication by time and type of stroke by time were statistically insignificant at 5% level of significance. Initially we avoid non-significant variables one by one starting from the most non-significant variable then compared the two nested models using AIC. First remove the interaction terms history of diabetic mellitus by time, having the most insignificant effect (p-value= 0.9973). The model was refitted after removing interaction terms history of diabetic mellitus by time and the AIC dropped from 8115.913 to 8110.707 indicating a better fit. The model was fitted again and the term stroke complication by time was still insignificant with a p-

value of 0.864 thus removed from the model. The model was fitted again and the AIC dropped from 8110.707 to 8104.855. The procedure should be continued until no variables to be removed from the model. Hence the reduced model with small number of parameter is preferred. The final linear mixed model for Glasgow Coma Scale is given by:

$$Y_i = 10.5 - 0.362Gen_i - 0.748Hh_i + 0.569Scom_i + 0.306Hd_i + 0.019Age_i + 0.604T_{ij} - (0.005Age_i)$$

Hence, the inferences for including the random effects model are not similar to those of the fixed effect model in terms of magnitude. However, according to the AIC including the random effects component is better than the fixed effect model.

4.2.3. Selecting Correlation Structure for GCS

In longitudinal study selecting best model is not selecting model with only the best mean structure, but also correlation structure. Among different correlation functions or correlation structure classes, in this study the most common correlation structures; compound symmetric covariance models and autoregressive structure of order one or AR (1) were used and compared. The small AIC value indicated that the model with autoregressive structure of order one is preferable for GCS, as shown in Table 4.3.

Table 4.3: Comparison of model with different correlation function for GCS

Model	AIC	BIC
AR. Model.	7890.538	7963.753
Comsymm. Model	8057.331	8130.546

Source: Jimma University Medical center, Ethiopia from January, 2020 to December, 2021

AR.Model=autoregressive structure of order one or AR (1), Comsymm.Model=compound symmetric covariance models

Therefore, for the data set of this study linear mixed model with autoregressive structure of order one can be considered as best final model for the response variables.

Table 4.4: Parameter estimates and standard errors for the linear mixed effects models of the GCS comes for the final model

Parameter	Estimates	SE	P-value	95% CI
(Intercept)	10.546	0.792	0.000	[8.994,12.098]
SBP	0.022	0.122	0.430	[-0.261, 217]
Gender (Male)	0.408	0.161	0.016	[-0.724, 0.092]
History hypertension(Yes)	-0.536	0.241	0.037	[0.064, 1.008]
Stroke complication (Yes)	-0.476	0.149	0.001	[0.184, 0.768]
History of diabetic (Yes)	-0.298	0.131	0.038	[0.041, 0.555]
Age	-0.316	0.112	0.019	[1.100, 1.709]
TM	0.403	0.119	0.000	[0.170, 0.636]
Age: TM	0.004	0.003	0.048	[-0.010, 0.002]
AIC: 7890.538	BIC:7963.753	LogLik:3932.269		

Random effects			Correlation Structure: AR(1)
	StdDev	Corr	
(Intercept)	2.406	(Intr)	Parameter estimate(s):
TM	0.346	-0.676	Phi = 0.647
Residual	1.775		

The estimated parameter for intercept of GCS is 10.546 with standard error of 0.792 represents an estimate of the average level of GCS during the first follow up time. Systolic blood pressure is not significant at baseline; this means that there was no statistically significant difference in GCS measures at baseline for stroke patients. The gender of patients was significant factor for the change of GCS (consciousness) of the stroke patients. This result reveals that, male patients had a 0.408 times increment in their average of consciousness of stroke than female patients. That is, the female patients had a lower consciousness than the male patients. Patient's history of hypertension at baseline of follow up had a 0.536 times decrement in average of GCS than those

patients who do not have history of hypertension at baseline. This result reveals that history of hypertension at baseline of follow up had decreases consciousness of stroke than those patients who do not have history of hypertension at baseline. Patients who had stroke complication at baseline had a 0.476 times decrement in average of consciousness of stroke than those who didn't had stroke complication at baseline. Concerning the patient baseline history of diabetic mellitus, it was the significant covariate for consciousness and those patients with the diabetic mellitus at baseline had a 0.298 times decrement in averages of consciousness than those patients doesn't have a history of diabetic mellitus at baseline visit.

With regarding to the age of the stroke patients at baseline, it had negatively associated significant effect on the change of consciousness for the stroke patients. This implies that one year increases in age of stroke patients was associated with a normal decreases by 0.316 of consciousness of stroke patients. As it stated previously, the observation time was significant covariates for consciousness of stroke patients; this implies a month increase in time was associated with increments in consciousness of stroke by 0.403.

Finally the parameter estimate of the interaction for age and time is 0. 004 which implies that the average rate of increase is related to age. In other words, younger patients have the higher rate of change in GCS measure than older patients.

The intercept of the random effects for GCS indicates there is variability between subjects at base line. And the slope of random effects for GCS indicates there is variability within subjects over time. The correlation -0.676 indicates, there is a negative correlation between intercept and slope of linear time effect for the random part GCS.

In addition, from the random effects, the residual terms=1.775 indicates that variation within the stroke patients in different time of GCS measurements. Phi = 0.647 shows In the First-order autoregressive structure AR(1) it is assumed that the correlation between time points decrease as the distances in time increase, this implies that the number of time intervals between pairs of observation increases, the correlation decreases and approaches to zero. Measurements that are closer in time have higher correlation than measurements with longer time between them

4.2.4. Model Diagnostics

Residual versus fitted value plots in (Appendix), we can see that the residuals seem to be randomly distributed with constant variance, since plot does not show any systematic pattern. Thus, it meets the assumption of error term. Q-Q plots for normality of random effects for GCS outcomes are also given in Figure 4 of the same Appendix; which illustrates the random effects are normally distributed with mean zero and variance covariance matrix.

4.3. Discussion

According to this study Age, systolic and diastolic blood pressure, time, gender, place of residence, history of hypertension, history of diabetes, history of heart disease, history of stroke complications, type of stroke and history of HIV/AIDS were the factors taken into account in this study. For the change in GCS, implies increase or decrease of stroke, the linear mixed mode identified baseline age, history of hypertension, stroke complications, history of diabetes, were considered as negatively risk factors(decreases the consciousness of stroke patients). However, gender (male), place of residence, history of HIV/AIDS, history of heart disease , time, and time their interaction were found to be positive associated with GCS.

The Glasgow Coma Scale was analysed using a linear mixed model. It was first necessary to comprehend the data structure and choose the appropriate modelling methodologies before fitting the linear mixed model. We noted that the Glasgow coma scale varied both among and between individuals based on the profile plot of each participant. The exploratory analysis's conclusion for mean structure (a Loess smooth curve) also indicated that, on average, Glasgow coma scale measurements tend to rise slightly linearly over time.

According to the study, women affected by stroke more than men because more women experience strokes throughout the course of their lives. This may be because more women experience strokes throughout the course of their lives and because women have particular risk factors for stroke, such as elevated blood pressure during pregnancy. This result is in line with research (10).Additionally, the study found that stroke patients who had hypertension at baseline typically had lower consciousness of stroke than stroke patients who did not. This might be because hypertension makes the heart work harder and, over time, harms the organs and arteries. Higher blood pressure (hypertension) increases the risk of having a stroke compared

to persons with normal blood pressure. This concurs with the earlier investigation (25).In a similar vein, this study demonstrates that patients with stroke complications typically began with lower consciousness than patients with no stroke complications. This result is in line with earlier research (31). According to this study, people with diabetes mellitus initially had lower consciousness than those who did not have the condition. This could be as a result of increased fatty deposits or blood clots in blood vessels brought on by long-term high blood glucose levels. These clots can constrict or obstruct blood vessels in the neck or brain, cutting off the blood supply and preventing oxygen from reaching the brain, leading to a stroke. The results of this study are consistent with earlier research (12).This result implied that age was linked to a typical rise in GCS. This may be not a result of the fact that as we age, our arteries gradually become harder and narrower. Additionally, atherosclerosis, which is a fatty substance buildup, is more prone to occur. The recent discovery is consistent with some earlier studies

CHAPTER FIVE

5. Conclusion and Recommendation

5.1. Conclusion

This study revealed that some variables such as baseline age, history of hypertension, stroke complications, history of diabetes, time, gender (male), place of residence, history of HIV/AIDS, history of heart disease and time interactions with baseline age were significant association with the changes of GCS of the stroke patients.

The result shows that being hypertensive, older, having diabetic mellitus and having stroke complication and Age were significantly decrease the consciousness level of the stroke patients. Moreover, on average GCS measure increase in a linear pattern over time. This implies as time increases the consciousness level of the stroke patients also increases (good). However being male and the time interactions with baseline age were significantly increases the consciousness level of the stroke patients.

5.2. Recommendation

Based on the findings of the study, the researcher recommends the following points to the concerned body.

- ☞ As having hypertension and diabetes mellitus decreases the average of consciousness) of stroke patients, managing high blood pressure and blood sugar levels may be able to delay the commencement of the Glasgow coma scale's decreases.
- ☞ As begin female and older age have substantial decreases the consciousness, it is imperative that women and elderly stroke patients receive specific care.
- ☞ Controlling such complications may help patients avoid having a stroke for an extended period of time because having a stroke complication generally decreases consciousness of stroke patients.

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Appendix

Table 1: Fixed effects component with all covariates with the corresponding estimates and time interactions for GCS.

	Estimate	SE	P-value
(Intercept)	1.081e+01	1.185e+00	< 0.001***
Age	1.864e-02	7.934e-03	0.019 *
genderMale	-3.332e-01	2.518e-01	0.186
resdRural	-1.867e-01	2.422e-01	0.441
TSischemic	-5.496e-01	2.398e-01	0.022 *
HNTYes	2.979e-01	1.308e-01	0.038*
DMYes	2.545e-01	1.829e-01	0.021*
HHDYes	1.845e-01	3.204e-01	0.565
SBP	-1.565e-02	6.401e-03	0.015*
DBP	2.051e-02	1.014e-02	0.043*
SCPLYes	1.017e+00	4.621e-01	0.028 *
HHIVYes	9.527e-02	4.110e-01	0.817
TM	8.257e-01	2.435e-01	0.000***
Age:TM	-4.750e-03	1.623e-03	0.003 **
genderMale:TM	4.998e-03	5.436e-02	0.927
resdRural: TM	-3.294e-02	5.067e-02	0.516
TSischemic:TM	1.007e-01	5.042e-02	0.046*
HNTYes:TM	3.265e-02	9.439e-02	0.729
DMYes:TM	-4.485e-02	5.864e-02	0.444
HHDYes:TM	-5.684e-02	6.713e-02	0.397
SBP:TM	-9.767e-06	1.312e-03	0.994
DBP:TM	-3.158e-03	1.848e-03	0.088
SCPLYes:TM	-2.044e-01	8.600e-02	0.018*
HHIVYes:TM	-1.246e-01	8.724e-02	0.153
AIC= 9787.198			

Table 2: Linear Mixed effects model with all covariates with the corresponding estimates and time interaction for GCS

effect	estimate	SE	p-value
(Intercept)	10.503	1.056	0.000
SBP	-0.006	0.002	0.007
genderMale	-0.362	0.265	0.171
HHIVYes	-0.216	0.366	0.554
HNTYes	0.748	0.452	0.098
Age	0.019	0.012	0.123
resdRural	-0.3378	0.366	0.356
TSischemic	-0.107	0.353	0.762
DMYes	0.203	0.410	0.621
HHDYes	0.306	0.468	0.513
DBP	0.0069	0.006	0.268
SCPLYes	0.569	0.291	0.051
TM	0.604	0.185	0.001
Age:TM	-0.005	0.002	0.037
resdRural:TM	-0.0355	0.070	0.621
TSischemic:TM	-0.017	0.066	0.798
DMYes:TM	0.001	0.080	0.997
HHDYes:TM	-0.066	0.093	0.482
DBP:TM	-0.002	0.001	0.294
SCPLYes:TM	0.010	0.057	0.861

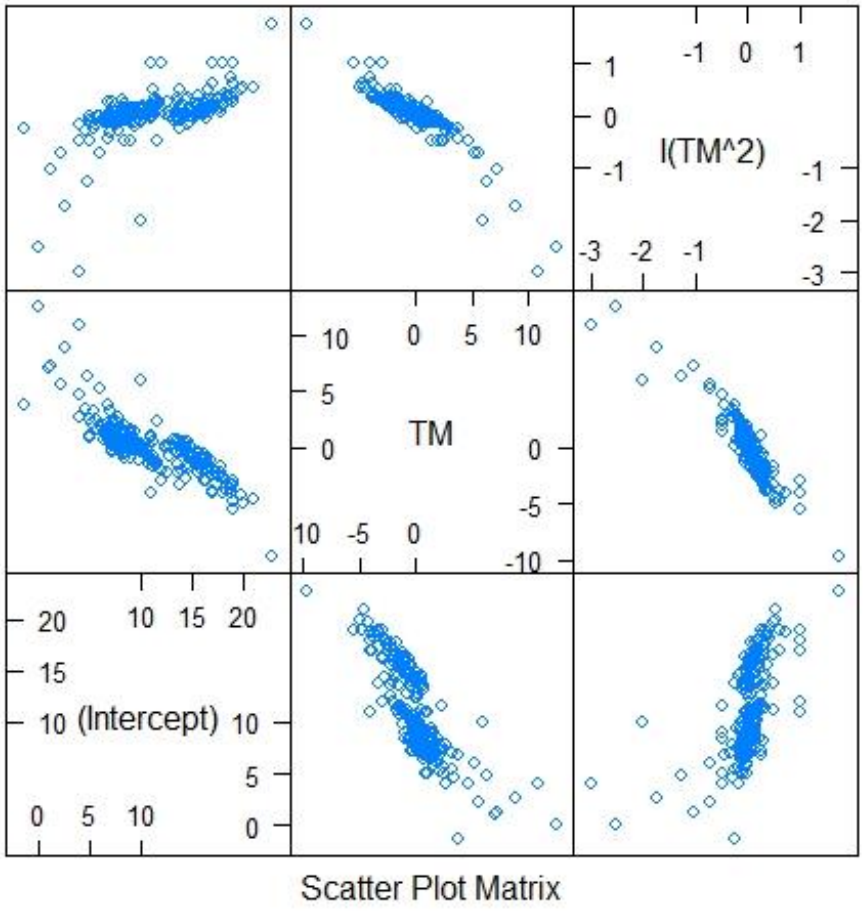

Figure 1: Random effect coefficient of lmList of Stroke patients.

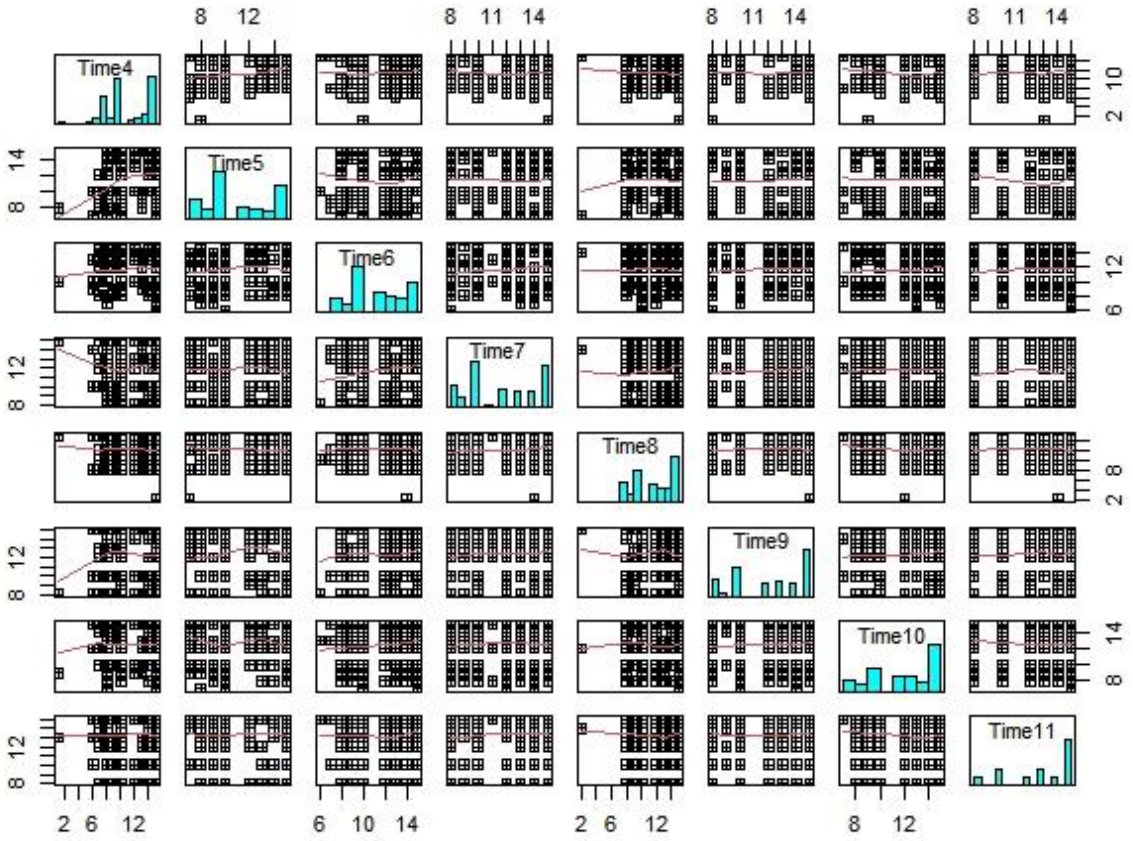

Figure 2: The scatter plot for correlation matrix between GCS of patients at each time points

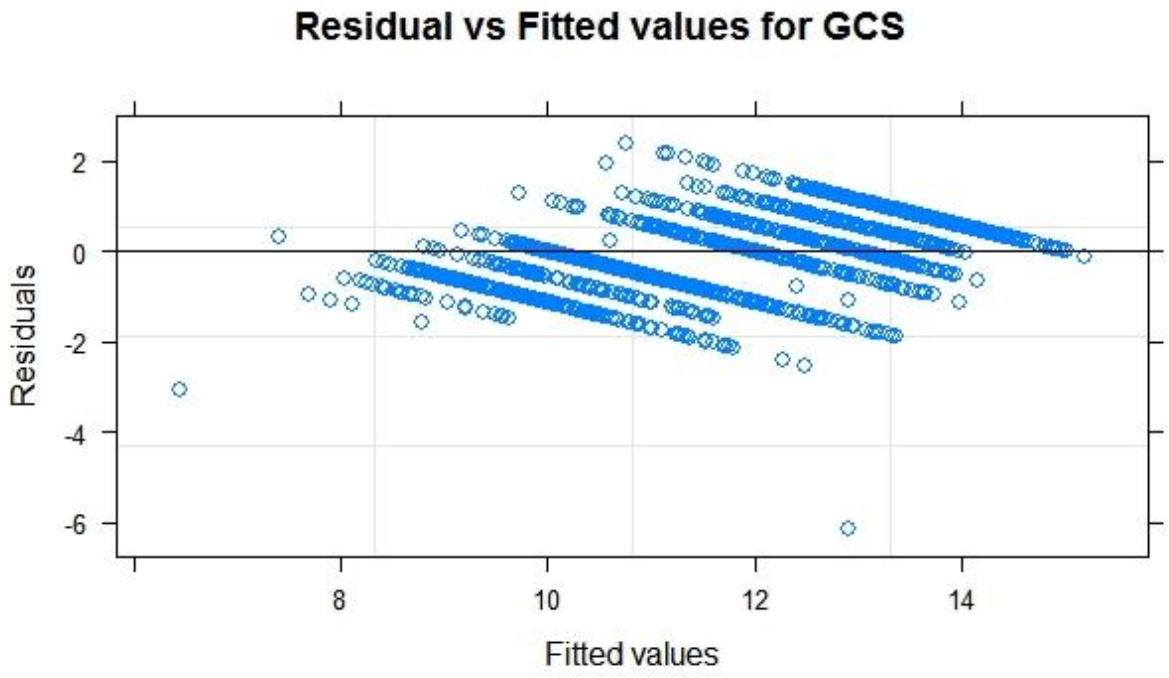

Figure 3: Q-Q plots for random intercept and slopes

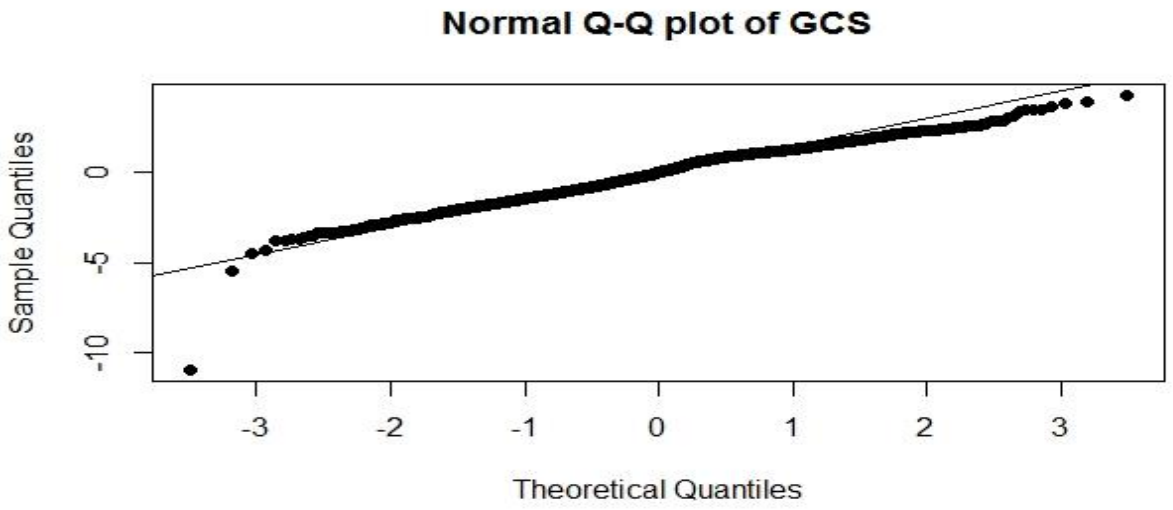

Figure 4: Residuals vs fitted value