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Time to Death and Its Predictors Among Stroke Patients Admitted to Felege Hiwot Comprehensive Specialized Hospital, Northwest Ethiopia, Retrospective Cohort Study, þÿ J a n u a r y / 2 0 1 9 N o v e m b e r / 2 0 2 0

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BAHIR DAR UNIVERSITY

COLLEGE OF MEDICINE AND HEALTH SCIENCES, SCHOOL OF PUBLIC HEALTH, DEPARTMENT OF EPIDEMIOLOGY AND BIOSTATISTICS

TIME TO DEATH AND ITS PREDICTORS AMONG STROKE PATIENTS ADMITTED TO FELEGE HIWOT COMPREHENSIVE SPECIALIZED HOSPITAL, NORTHWEST ETHIOPIA, RETROSPECTIVE COHORT STUDY, JANUARY/2019 – NOVEMBER/2020

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JULY, 2021

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A THESIS SUBMITTED TO THE DEPARTMENT OF EPIDEMIOLOGY AND BIOSTATISTICS, SCHOOL OF PUBLIC HEALTH, COLLEGE OF MEDICINE AND HEALTH SCIENCES, BAHIR DAR UNIVERSITY; IN PARTIAL FULFILLMENT OF THE REQUIRMENTS FOR THE DEGREE OF MASTERS IN EPIDEMIOLOGY

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Declaration form

Declaration

This is to certify that the thesis entitled **"Time to death and its predictors among stroke patients admitted to Felege Hiwot comprehensive specialized hospital, Northwest Ethiopia"**, submitted in partial fulfillment of the requirements for the degree of Master of Epidemiology in Department of Epidemiology and Biostatistics, School of Public Health, Bahir Dar University, is a record of original work carried out by me and has never been submitted to this or any other institution to get any other degree or certificates. The assistance and help I received during the course of this investigation have been duly acknowledged.

Name of the candidate	Date	Signature

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Advisor's approval form

I hereby certify that I have supervised, read, and evaluated this thesis titled **"Time to death and predictors among stroke patients admitted to Felege Hiwot comprehensive specialized hospital, Northwest Ethiopia"** by Betelhem Tajebe prepared under my guidance. I recommend the thesis for final submission.

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Examiner's approval form

We hereby certify that we have examined this thesis entitled **"Time to death and predictors among stroke patients admitted to Felege Hiwot comprehensive specialized hospital, Northwest Ethiopia"** by Betelhem Tajebe. We recommend and approve the thesis a degree of "Master of Epidemiology"

Board of Examiner

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Internal examiner's name	Signature	Date

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Abstract

Introduction: Worldwide, stroke is a leading cause of mortality and disability. In Ethiopia, stroke is one of the diseases in the top five which causes death. In Felege hiwot comprehensive specialized hospital, for the last four years stroke has been the leading cause of hospital admission and death. From previous studies some of the modifiable factors like hypertension, heart disease reported as the cause of early mortality among stroke patients. However, the effect of behavioral factors on time to death among stroke patients did not addressed which is include in the current study.

Objective: To assess the time to death and its predictors among stroke patients admitted to Felege Hiwot Comprehensive Specialised Hospital, Northwest, Ethiopia

Methods: An institution based retrospective follow-up study was conducted at Flege Hiwot comprehensive specialized hospital from January 2019 – November 2020. Simple random sampling technique was used to select 435 study participants. Data abstraction sheet was used, which is adopted from different literatures. Data was entered using EpiData version 3.1 and analyzed in STATA version 14 software. Mortality rate of stroke and median time to death was estimated. During bivariate analysis, P value < 0.2 was used as a cutoff point for including predictors in the multivariable model. Numerical and graphical tests was used to check proportional hazard assumption. If one of the tests violated the assumption, Frailty model would be used for the analysis. Lognormal Frailty model was used for the analysis. In multivariable analysis, variables with p-value <0.05 declared as predictor of time to death in stroke patients.

Result: Mortality rate of admitted stroke patients was 22% and median time to death was 19 days. The total individual person time was 2,392 person-day. Hemorrhagic stroke [AHR 1.8 (95% CI, 1.02-3.3)], Glasgow coma scale < 8 [AHR 4.8 (95% CI, 2.35-9.83)], aspirated pneumonia [AHR 3.47 (95% CI, 1.97-6.13)] and increased intracranial pressure [AHR 2.3 (95% CI, 1.34-4.94)] were statistically significance predictors of time to death among admitted stroke patients.

Conclusion and Recommendation: The cumulative incidence rate among stroke patients was 22%. The mortality rate of stroke is higher than previous studies conducted in Ethiopia. Early identification and management of stroke and stroke related complication should be done.

Key words: Mortality, Predictor, Stroke, Time to death

Acronyms and Abbreviations

ABM	Abnormal Body Movement
AFT	Accelerated Failure Time
AIC	Akaike Information Criterion
AHR	Adjusted Hazard Ratio
AOR	Adjust Odd Ratio
AP	Aspirated Pneumonia
CI	Confidence Interval
CT	Computerized Tomography
CHR	Crude Hazard Ratio
DALYs	Disability Adjusted Life Years
ECG	Electrocardiogram
FHCSH	Felege Hiwot Comprehensive Specialized Hospital
GBD	Global Burden of Disease
GCS	Glasgow Coma Scale
HMIS	Health Management Information System
ICP	Intracranial Pressure
LMICs	Low- and Middle-Income Countries
mm/hg	Millimeter Per Mercury
MRI	Magnetic Resonance Imaging
MRN	Medical Record Number
PH	Proportional Hazard
P-value	Measures of Probability

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1. Introduction

1.1 Background

WHO define stroke as rapidly developed clinical signs of focal or global disturbance of cerebral function, lasting more than 24 hours or until death, with no apparent non-vascular cause (1). It is permanent (i.e. irreversible) death of neurons caused by inadequate perfusion of a region of brain or brain stem leading to death with no apparent cause other than vascular origin (2, 3).

There are two main types of strokes. Ischemic stroke (IS) which is the most common type and results when acute occlusion of an intracranial vessel causes reduction in blood flow to the brain region it supplies. Etiologies of IS are thrombotic and embolic. Hemorrhagic stroke (HS) occurs due to intracranial bleeding or rupture of blood vessels with in brain. Etiologies are hypertension, severe headache and other (vascular aneurism and anticoagulant related). HS is more severe and causes higher risk of mortality, and about 85% of all strokes are ischemic (1, 4, 5).

The clinical manifestations of stroke are highly variable because of the complex anatomy of the brain and its vasculature (2). Focal weakness, speech disturbance, loss of vision, severe headache, and paresis of arm, and leg most often one side of the body are some of the clinical manifestations of stroke. It results from inadequate supply of blood supply and damage to the brain tissue (4, 6)

History, physical examination, laboratory findings and imaging studies are very crucial for the diagnosis of stroke. Computed tomography scan (CT scan) and magnetic resonance imaging (MRI) are widely used to support the diagnosis of stroke (5, 7). In most developing countries, CT scan or MRI are not usually available and affordable (9).

Treatments of stroke depend on the type of stroke. The objective of treatment is to reverse or lessen the amount of tissue infarction and improve clinical outcome. Management of stroke includes supportive treatment (coma care), medication (antiplatelet, anticoagulants, lipid-lowering agents), and physiotherapy. Early management of stroke reduce in-hospital mortality, complication, and length of hospital stay (1, 10, 11).

1.2 Statement of the Problem

Globally, stroke is a leading cause of mortality and disability. Around 15 million people suffer from stroke each year. Among these, five million die and another five million are permanently disabled. Four out of five strokes occur in the low- and middle-income countries (LMICs) who can least afford to manage the consequences of this disease (11, 12).

In 2019 worldwide prevalence of stroke cases is 101 million. According to global burden of disease (GBD) report, in 2019 there are 12.2 million new stroke cases, from this 62.4% was IS. Next to ischemic heart disease, stroke is the second cause of death which is 6.55 million deaths due to stroke (14). Stroke is the second causes of global disability and more than 87% of disability estimated to occur in LMICs. The disability caused by HS is higher than IS (12). In addition, stroke is the largest contributor (42·2%) to global neurological disability adjusted life years (DALYs) (3).

The global burden of stroke has been increasing over the years. In high-income and low-income countries, from 1990 to 2017 incidence of stroke increased by 33% and 69% respectively. In high-income countries, stroke mortality had been decreased from 1990 to 2017 by 12%. Whereas in low-income countries stroke mortality had been increased by 40% (6, 11).

In high-income countries, as a result of improved healthcare (including screening, prevention, diagnosis, and treatment) and general awareness about stroke decreases stroke mortality. Though, in low-income countries, due to poor health care system and the changes in social, economic, demographic and epidemiological pattern among the population increases the incidence and mortality of stroke. The burden of stroke is higher in low-income countries than in high income countries. However, the overall rate of stroke remains high due to the aging of the population (10, 14, 15, 16).

Risk factors of stroke mortality classified as non-modifiable and modifiable. The non-modifiable risk factors are age, sex, family history and race/ethnicity. The modifiable risk factors are hypertension, diabetes mellitus (DM), high blood cholesterol, cardiovascular disease, atrial fibrillation, smoking, alcohol consumption, obesity, diet, and physical inactivity (4, 5, 6).

The outcomes of stroke range from full recovery to severe disability and death, and it causes significant personal, household and societal burdens (19). In addition, stroke survivors may suffer from disabilities, requiring temporary or lifelong assistance, resulting in an enormous burden, both in human and economic costs (12).

In different countries of Africa, studies had been conducted on prevalence and associated factors of stroke mortality. In Africa, stroke mortality rate during hospitalization ranges from 12% - 43.4% (12, 13, 14, 15, 16). Most patients discharged with significant neurologic deficit (24, 25). Among in-hospital deaths, the majority are patients with hemorrhage stroke than ischemic stroke (22, 23, 24).

In Ethiopia, Stroke is a frequent cause of morbidity and mortality (5). Most stroke deaths occurred early after admission due to stroke related acute medical and neurological complications. Nearly one-fifth of stroke patients have been died during hospitalization (27). Because of pre-hospital delay and poor standard of care increases the in-hospital mortality and majority of the patients were discharged with severe physical disability (20).

A systematic review and meta-analysis conducted in Ethiopia identifies the pooled stroke mortality during admission period is 18% (27). Recent studies conducted in differ towns of Ethiopia shows different mortality rate among stroke patients ranges 12.5% - 28.33% (6, 18, 24).

In Ethiopia different studies conducted on the magnitude and the associated factors of stroke. However, little information is available regarding to the median time of in-hospital mortality in both types of stroke (ischemic and hemorrhagic stroke) during admission period, especially in the study area. In the Felege-Hiwot Comprehensive Specialized Hospital (FHCSH) stroke is the leading cause of hospital admission and in hospital mortality for the last years. This study will give an idea on the time to death among both types of stroke patients and will add the effect of some behavioral factors on time to death, which is not assessed by previous studies.

1.3 Significance of the study

Evaluation and better understanding of the survival status and predictor of survival might used to reduce mortality, complications and improves the quality of care given for stroke patients. This study could help clinicians and other service providers in designing interventions to reduce earlier mortality, by providing more targeted interventions in high-risk patients.

This study could also help policy makers in designing appropriate strategies for addressing the traditional modifiable risk factors of stroke. After all, this study would help researchers and the scientific community in updating their knowledge on predictors of time to death among stroke patients and it would serve as baseline information for future research.

2 Literature review

2.1 Time to death among admitted stroke patients

Studies conducted in Brazil, and Malaysia revealed that mortality rate among stroke patients were 20.6% and 23.6% respectively (29, 30). Studies done in Africa Cameroon, Sierra Leone and Burkina Faso shows that mortality rate among admitted stroke patients were from 26.8% - 34.8% (22, 31, 32, 28). Higher mortality rate reported among Sierra Leoneans stroke patients.

Studies conducted in Ethiopia provide that mortality rate among admitted stroke patients were ranges from 11% - 22.2% (7, 20, 25, 33, 34). In this studies the median time of in hospital mortality following admission were 4.38 days and 3 days respectively (20, 25).

2.2 Socio demographic factors and patient survival

A study conducted in Malaysia found that, the relative hazard of early mortality among old age stroke patients were higher than those who were young age stroke patients (30). Also a study conducted in Brazil provided that, old age stroke patients were 1.3 times more likely to had poor treatment outcome at discharge when compared to young age stroke patients (29). A study conducted in Benin shows, stroke patients who were at their advanced age increased the risk of mortality by 7.73 times than their counterparts (35). Studies done in Ethiopia shows, stroke patients whose age were more than 50 years old were 3.3 times more likely to end up with poor treatment outcome than stroke patients who were younger than 50 years old (36) and other study shows younger patients (≤50 years old) were 59% times less likely to get stroke when compared to their counterparts (6).

The relative hazard of mortality among male stroke patients was 78.2% lower than female stroke patients (30). In addition, another study shows that the risk of poor treatment outcome among male stroke patients were 60% lower than female stroke patients (29). Similar finding in a study conducted in Zambia shows that female stroke patient increased the risk of mortality by 2 times when compared to male stroke patients (37).

2.3 Risk factors and patient survival

A study conducted in Malaysia shows that the probability of death among stroke patients who had rheumatic heart disease were six times higher than those patients who did not have rheumatic heart disease (30). A study conducted in Burkina Faso found that, stroke patients who had cardiac comorbidities increased risk of early mortality by 6.4 times than those who did not had cardiac comorbidities (31). Studies conducted in Ethiopia show that, cardiac patients increased the risk of acquiring stroke when compared to their counterparts (5, 38).

A study conducted in Cameroon shows that, patients with elevated systolic pressure increased risk of mortality than patients with normal systolic blood pressure (39). A study conducted in Bahir Dar, Ethiopia found that, the odds of acquiring stroke among hypertensive patients were three times more than their counter parts and also diabetic patients were 3 times more likely to acquire stroke when compared with non - diabetic patients (6). Although another study found that, risk of early mortality among diabetes patients lower by 35% than non-diabetes patients (28).

Studies conducted in Ethiopia found that stroke patients who had atrial fibrillation, decreases risk of hemorrhagic stroke by 92% when compared to risk of ischemic stroke (5). Another, study also reveals that, rate of survival among patients who develop atrial fibrillation reduced by 38% when compared to their counterparts (28). In the contrary, stroke patients who had atrial fibrillation increased the risk of mortality when compared to their counterparts (24).

A study conducted in Ethiopia, St. Paul Hospital, shows patients who had a previous history of stroke increased the risk of acquiring stroke than patients who did not have (24). A study conducted in Bahir Dar shows that, patients who had previous ischemic stroke were 2 times more likely to die early when compared to those who did not have previous ischemic stroke (28).

2.4 Behavioral factors and patient survival

A study conducted in Malaysia found that stroke patients who were ever smoker and current smoker increased risk of mortality by 4.4 and 4.2 times respectively than the never smokers (30). Another study conducted in China shows patients who were current smoker increased risk of stroke 1.39 times than patients who were never or ever smokers (40). In addition, a study conducted in Saudi Arabia shows current smokers were 2.4 times more likely to die early than the non-smokers (41).

A study conducted in Cuba found that patients who had past alcoholic habit were 3.5 times more likely to acquire stroke when compared to their counterparts (42). Also, a study conducted in Bahir Dar shows that patient who drank alcohol increased the risk of stroke by 2 times than patients who didn't drink alcohol (6).

2.5 Neurological factor and patient survival

Study conducted in Cameroon shows, stroke patients with Glasgow Coma Scale (GCS) <8 were 13.4 times more likely to die early than patients with GCS ≥8 (22). Also a study conducted in Uganda and Ethiopia shows, stroke patients who had GCS <8 increased risk of stroke when compared to their counterparts (36, 37). In addition, in another study found that, stroke patients who had sever (3-8) record of GCS at admission increased the risk of mortality when compared to their counterparts (25).

A study conducted by Nkoke et al shows the risk of dying early was six times higher in hemorrhagic stroke patients when compared to ischemic stroke patients (22). In addition, a study in Zambia shows being patient of hemorrhagic stroke increased the risk of mortality 3 times when compared to patients with ischemic stroke (37). Also, a study conducted in Ethiopia shows that, the risk of dying after hemorrhagic stroke is about four times higher than after ischemic stroke (43).

Patients who had a chief complaint of hemiplegia were 0.75 times less likely to have poor treatment outcome than other complaints (36). Also patients who had aphasia almost six times more likely to die early than patients who did not have (35)

2.6 Patient presentation and their survival

A study conducted in Cameroon shows that, stroke patient who had hyperglycemia during admission were four times more likely to die early than their counterpart (22). Similarly, the study conducted in Malaysia shows the probability of mortality among stroke patients who had elevated random blood sugar were 9.3% times higher than their counter parts (30).

A study conducted in Ethiopia shows patients who had raised intracranial pressure (ICP) were 6 times more likely to decrease the survival time when compared to their counterparts (20). The probability of early mortality among patients who had brain edema increased four times than patients who did not have brain edema (45).

Patients who developed urine incontinence during initial hospital presentation were 3.5 times more likely to die early when compared to their counterparts (20). A study conducted in Zambia shows that, patients who developed pneumonia increased risk of mortality by 25.5 times than those who did not have pneumonia (37).

The risk of early mortality among stroke patients who diagnosed clinically alone without imaging confirmation increases than stroke patients who diagnosed by imaging modalities (16, 38). Stroke patients who treated with aspirin were increased survival by 56% when compared to patients who did not treat with aspirin (30). Stroke patients who stays in hospital more than 5 days had 2 times more the risk of poor treatment outcome when compared to their counter parts (16).

3 Conceptual framework

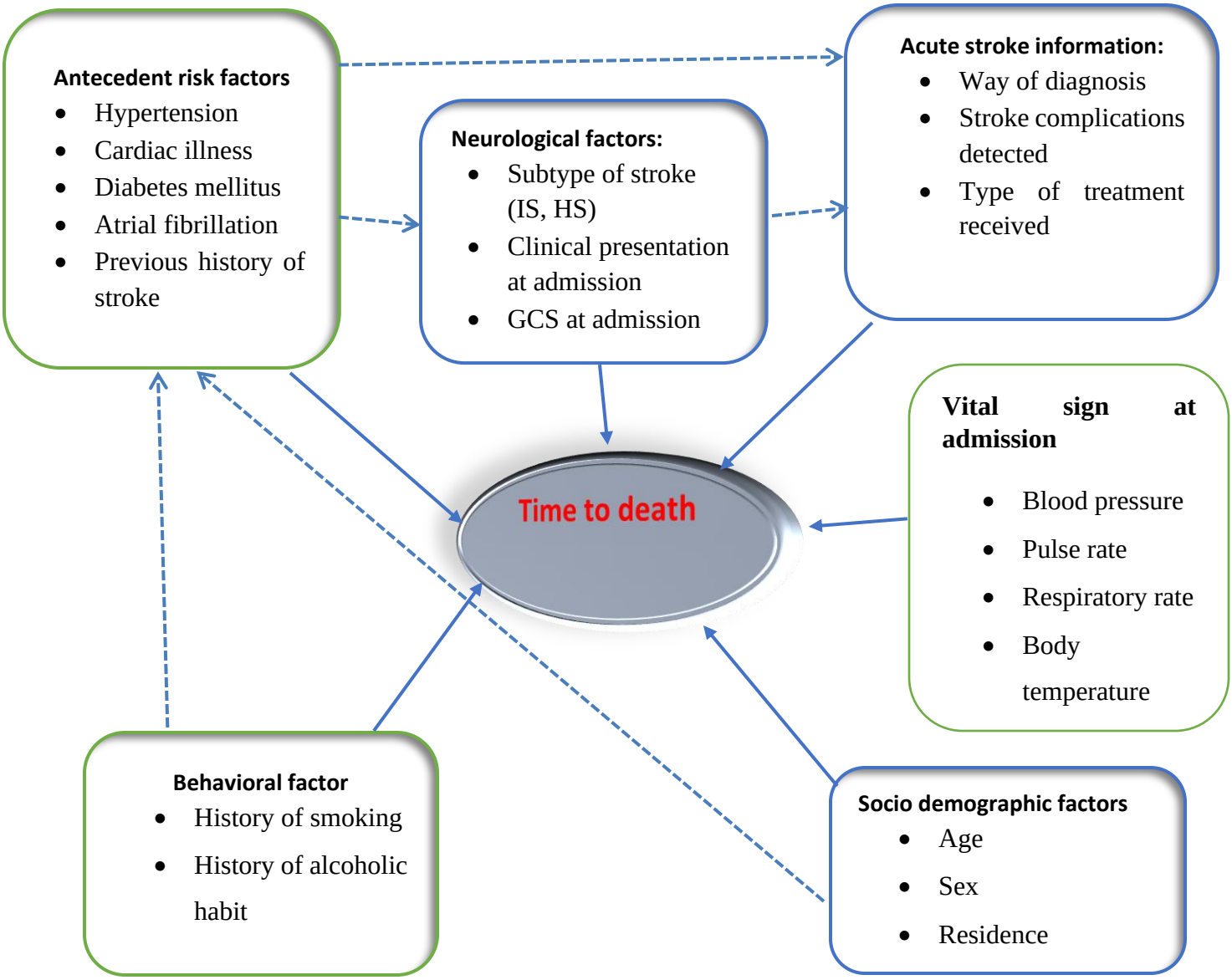

Figure 1 Conceptual framework to determine time to death among admitted stroke patients

4 Objective

4.1 General objective

- To assess the time to death and its predictors among stroke patients admitted to Felege Hiwot Comprehensive Specialised Hospital, Northwest Ethiopia, January 1/2019 – November 30/2020

4.2 Specific objectives

- To estimate the mortality rate of stroke patients admitted to Felege Hiwot Comprehensive Specialised Hospital, Northwest Ethiopia
- To identify predictors of time to death among stroke patients admitted to Felege Hiwot Comprehensive Specialised Hospital, Northwest Ethiopia

5 Methods

5.1 Study area and period

5.1.1 Study area

The study was conducted in FHCSH, Bahir dar city, Northwest Ethiopia, which is 552 km away from Addis Ababa, the capital city of Ethiopia. It is one of the comprehensive specialized hospitals in Amhara region. It provides outpatients and inpatient medical services, with different sub-specialty departments including oncology, for 10 million population in its catchment area. The hospital has CT scan machine, and stroke patients can get non contrast brain CT imaging service with fee of 500 birr. The hospital has 474 beds, among these beds 80 of them are in medical ward. During the study period there were 6,770 admissions in medical ward and 1,448 (21.4%) were stroke cases.

5.1.2 Study period

An institutional based retrospective follow-up study was conducted among stroke patients who were admitted from January 1/2019 – November 30/2020 in FHCSH. The patient followed from first day of admission to the day of discharge. The data extracted on patient medical card from December 1 to 31, 2020.

5.2 Study design

Institution based retrospective follow-up study was conducted among admitted stroke patients from January 1/2019 – November 30/2020

5.3 Source and study population

5.3.1 Source population

All stroke patients who had admitted in FHCSH hospital with the primary diagnosis of stroke

5.3.2 Study population

All stroke patients who had admitted to FHCSH with the primary diagnosis of stroke from January 1/2019 – November 30/2020

5.4 Inclusion and Exclusion criteria

5.4.1 Inclusion criteria

All stroke patients who had admitted to FHCSH with the primary diagnosis of ischemic or hemorrhagic stroke from January 1/2019 – November 30/2020.

5.4.2 Exclusion criteria

All stroke patients who had admitted to FHCSH with the diagnosis of unspecified stroke and patients with incomplete medical card from January 1/2019 – November 30/2020.

5.5 Sample size calculation and Sampling techniques

5.5.1 Sample size calculation

The sample size was determined using two population proportion formula with the assumptions of 5 % significant level (two sided) test, 80% power, and 95% CI, ratio of non-exposed to exposed (R) 2:1 using Epi info version 7.2 software. By taking urinary incontinence of stroke patients as a exposure variable and with assumptions of percent of exposed with outcome =64%, percent of non- exposed with outcome =36% was used to calculate sample size (20). Finally, it became 126.

Using predictors from previous study, sample size was determined using STATA version 14.2 by taking three covariates from study conducted in Ethiopia (28). The covariates considered to be the most important risk factors were used to determine the sample size and the calculated sample size for each covariate listed in table 1.

Table 1: Sample size for covariates to determine time to death among stroke patient

Covariates	HR	Prob. of event	Sample size	Citation
Previous history of ischemic stroke	1.84	0.29	292	(28)
Heart disease	2.23	0.29	169	(28)
Hypertension	1.647	0.29	435	(28)

HR: Hazard ratio

Prob: Probability

The largest sample size was taken, which was 435.

5.5.2 Sampling technique

Health management information system (HMIS) registration was used as sampling frame. Simple random sampling technique was used to select patient medical record number among those who were admitted from January 1/2019 – November 30/2020 in FHCSH. Table of random number of simple random sampling technique was used to select the study participants. The selected medical number was used to abstract the relevant information from patient medical folder.

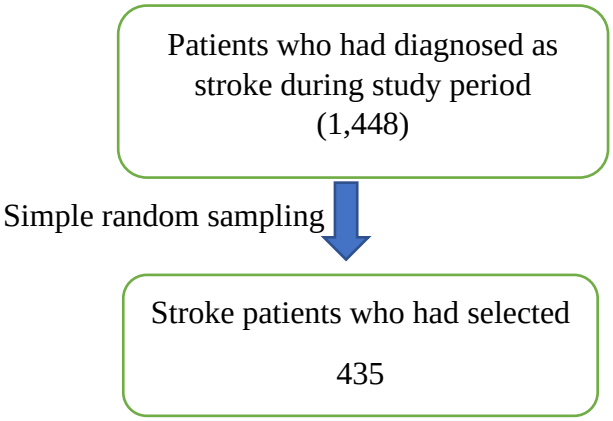

Figure 2: Sampling procedure for study participants in FHCSH, Northwest Ethiopia, January 2019 – November 2020

5.6 Variables in the study

5.6.1 Dependent variable

- Time to death among stroke patients (In days)

5.6.2 Independent variables

- Socio demographic variables: age, sex, and residence
- Antecedent risk factors: hypertension, diabetes mellitus, cardiac illness, atrial fibrillation, and previous history of stroke,
- Behavioral factor: history of smoking, and history of alcoholic habit
- Acute stroke information: way of diagnosis, vital signs at admission, stroke complications detected, type of treatment received, and treatment outcome at discharge
- Neurological factors: Subtype of stroke, clinical presentation at admission, and GCS score at admission,

5.7 Operational definition

Censored: Those subjects who were discharged against medical advice, discharged with medical advice with improvement or significant neurologic deficit, death other than stroke (accident or any cause not related to stroke), referred to other health facilities or alive until the end of the study whichever occurred first were considered as censored.

Death (Event): Stroke patients who were died in the hospital after admission and the cause of death related to stroke

Cardiac illness: a patient who have at least one of this disease ischemic heart diseases, rheumatic heart disease, hypertensive heart disease, valvular heart disease

Entry date: The date of admission taken from the patient medical record

Glasgow coma scale (GSC): Helps to measure level of consciousness (20).

- Poor GCS (≤8): Severe brain injury (unconscious)

- Moderate GCS (9–12): Moderate brain injury (drowsy)
- Good GCS (13–15): Mild brain injury (alert)

Time to Death (Event): The median time from first day of admission to the occurrence of adult stroke death within the admission period.

Time of onset of stroke: Is the time in hours when the patient or observer first became aware of stroke symptoms (1).

5.8 Data collection and quality assurance

5.8.1 Data collection

Data was collected using a data abstraction checklist. The checklist was developed after review of different literatures and previous similar studies, and organized to the objective of the study. It was prepared in English and contained five parts, socio-demographic characteristics of the patients, behavioral factors, antecedent factors of stroke, acute stroke symptoms, and neurological factor of stoke. Nurses were assigned as a data collector. The patient medical card was used as data sources. In addition, other clinical records including imaging results and any relevant investigation also used during the data abstraction.

5.8.2 Data quality control

The selection of data collectors was based on the possible familiarity in medical ward. Training was given for the data collectors and the supervisor about the objective of the study, process of the data abstraction and data abstraction checklist. The principal investigator was supervised the whole process of data abstraction.

To ensure the quality of data, the filled sheet was checked for completeness and consistency by the supervisor and principal investigator.

5.9 Data processing and management

After the data abstraction, the data was entered into EpiData version 3.1. The data was checked by the investigator if there is any error or incompleteness during data entry. The data was exported to STATA version 14 for analysis. After exporting data editing, cleaning and coding was done to make the data suitable for further analysis.

5.10 Statistical Analysis

A continuous variable was described in terms of their mean (SD), also the outcome and the categorical variables
were described in terms of their frequencies and percentage at baseline. The incidence rate of mortality among admitted stroke patients was calculated.

The proportional hazard (PH) assumption was checked, using global goodness of test and time dependents of predictors before fitting the final model.

The predictors of time to death were determined using Cox proportional hazard regression. Variables having P-value ≤ 0.20 during bivariate analysis were entered into the multi-variable analysis. A significance level of 0.05 was taken as cut-off points for all statistical tests.

5.11 Ethical consideration

Ethical clearance was obtained from Institutional Review Board of Bahir Dar University. Written permission was obtained from FHCSH research and quality assurance department before starting data collection. The data from the medical records handled with strong confidentiality, neither the case records nor the data extracted used for any other purpose and all the collected patient information stored anonymously.

6 Result

6.1 Sociodemographic characteristics

Among 435 participants, more than half of them were males and around three fourth of them were from rural area. The mean age of participants were 60.95 (±14.68) years old and more than half of stroke mortality occurred in patients whose age was greater than 65 years old (Table 2).

Table 2: Socio-demographic characteristics of stroke patients admitted in FHCSH, Northwest Ethiopia, January 2019 – November 2020

Variables	Categories	Survival status		
		Death (%)	Censored (%)	Total frequency
Age	<65	47 (21.20)	175 (78.8)	222
	≥65	49 (23)	164 (77)	213
Sex	Male	42(17.8)	194 (82.2)	236
	Female	54 (27.1)	145 (72.9)	199
Residence	Urban	22 (18)	100 (82)	122
	Rural	74 (23.6)	239 (76.4)	313

6.2 Risk factors

Among the participants more than half of them (56%) had history of hypertension and more than one tenth of them (12.6%) had cardiac illness. Atrial fibrillation and previous history of stroke were other risk factors for stroke patients next to hypertension and cardiac illness (Figure 3).

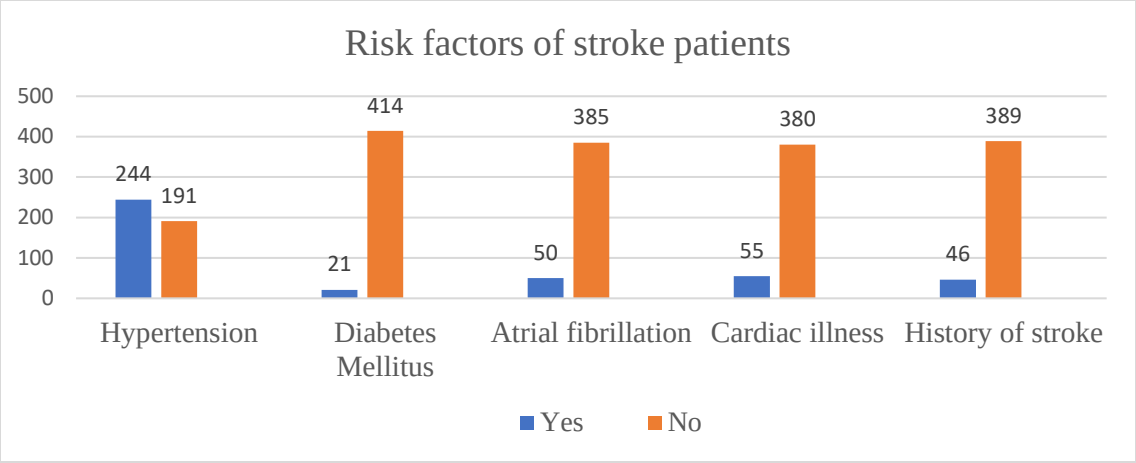

Figure 3: Bar graph of antecedent risk factors of stroke patients admitted in FHCSH, Northwest Ethiopia, January 2019 – November 2020

6.3 Behavioral factors

Among stroke patients admitted to the hospital eight (2%) had history of smoking and more than one tenth of participants (12%) had history of alcoholic habit (Figure 4).

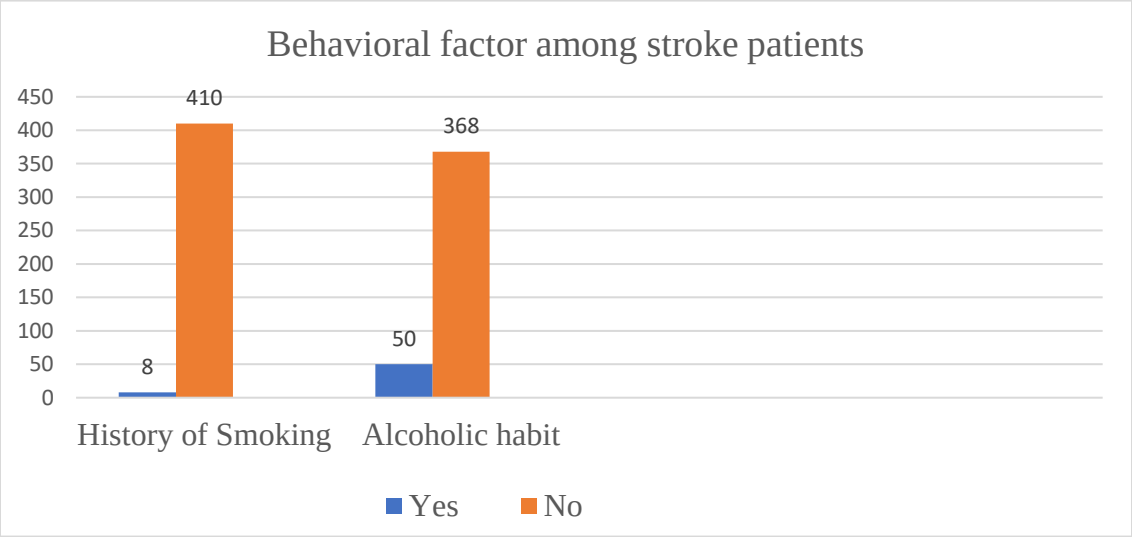

Figure 4: Plot of behavioral factors of stroke patients admitted in FHCSH, Northwest Ethiopia, January 2019 – November 2020

6.4 Neurological factors

Among 435 participants, more than two third of them (67.8%) were diagnosed as IS and, it was the more common type of stroke. Less than half of them (45.5%) had good level of consciousness with GCS score of 13-15. Concerning stroke patient's presentation during hospital arrival fourth five of them (80.9%) had hemiparesis and more than three five of them (62.1%) had aphasia. Other part of neurological factors can be found in the annex 2.

Table 3: Neurological factors of stroke patients admitted in FHCSH, Northwest Ethiopia, January 2019 – November 2020

Variables	Categories	Survival status		
		Death (%)	Censored (%)	Total frequency
Stroke type	Ischemic	45 (15.3)	249 (84.7)	294
	Hemorrhagic	51 (36.2)	98 (63.8)	141
GCS* during admission	Good	12 (6.1)	186 (93.9)	198
	Moderate	29 (19.6)	119 (80.4)	148
	Poor	55 (61.8)	34 (38.2)	89
Hemiplegia	Yes	7 (25.9)	20(74.1)	27
	No	89 (21.8)	319 (78.2)	408

* – Glasgow Coma Scale,

6.5 Acute stroke presentation

Among the participants, two third (66.3%) of them were arrived at hospital within the first 24 hours after developing symptoms of stroke. Most (93%) of the participants were diagnosed with the help of brain imaging. One hundred forty-three (34.2%) of participants had develop complication after admitted to the hospital. Other variables which are included in acute stroke presentation can be found in annex 3.

Table 4: Acute stroke presentation of stroke patients admitted in FHCSH, Northwest Ethiopia, January 2019 – November 2020

Variables	Categories	Survival status		
		Death (%)	Censored (%)	Total frequency
Hospital arrival	1-3hr	6 (31.6)	13 (68.4)	19
	4-24hr	74 (27.4)	196 (72.6)	270
	>24hr	16 (11)	130 (89)	146
AP*	Yes	77 (51)	74 (49)	151
	No	19 (6.7)	265 (93.3)	284
Way of diagnosis	Brain imaging	89 (22)	315 (78)	404
	Clinically	7 (22.6)	24 (77.4)	31

* – Aspirated pneumonia

During admission the mean ($\pm SD$) systolic and diastolic blood pressure of the participants were 147 (± 32) mm/Hg and 87 (± 19) mm/Hg respectively. Also, the mean ($\pm SD$) pulse rate and body temperature were 86 (± 18) and 36.4 (± 1) respectively.

Among participants more than two third of them (67.8%) were received anti-platelet and less than half of them (46.4%) were received antibiotics for prevention and treatment of stroke related infection and complication (Table 5).

Table 5: Treatment factors of stroke patients admitted in FHCSH, Northwest Ethiopia, January 2019 – November 2020

Variables	Categories	Survival status		
		Death (%)	Censored (%)	Total frequency
Anti- platelet	Yes	54 (18.3)	241 (81.7)	295
	No	42 (30)	98 (70)	140
Anti- coagulants	Yes	47 (19.6)	193 (80.4)	240
	No	49 (25.1)	146 (74.9)	195
Anti-hypertensive	Yes	45 (22)	160 (78)	205
	No	51 (22.2)	179 (77.8)	230
Statin	Yes	50 (17.5)	235 (82.5)	285
	No	46 (30.7)	104 (69.3)	150
Anti-diabetics	Yes	3 (13.6)	19 (86.4)	22
	No	93 (22.5)	320 (77.5)	413
Antibiotics	Yes	90 (44.5)	112 (55.5)	202
	No	6 (2.6)	227 (97.4)	233
Diuretics	Yes	28 (27.7)	73 (72.3)	101
	No	68 (20.4)	266 (79.6)	334

Anti-coagulants (Heparin, Warfarin), Anti-platelet (Aspirin, Clopidogrel), Anti-hypertensive (hydralazine, nifedipine, enalapril), Statin (atorvastatin, lovastatin), Anti-diabetics (Metformin), Antibiotics (Ceftriaxone, vancomycin), Diuretics (Mannitol, Lasix, Spironolactone)

6.6 Incidence of death

During follow up, admitted stroke patients who died in the hospital were 96 and the incidence rate was 4/100 stroke patient-days. The total person-time followed was 2,392 person-days. More than one fifth of the participants were left the hospital without medical advice (figure 5).

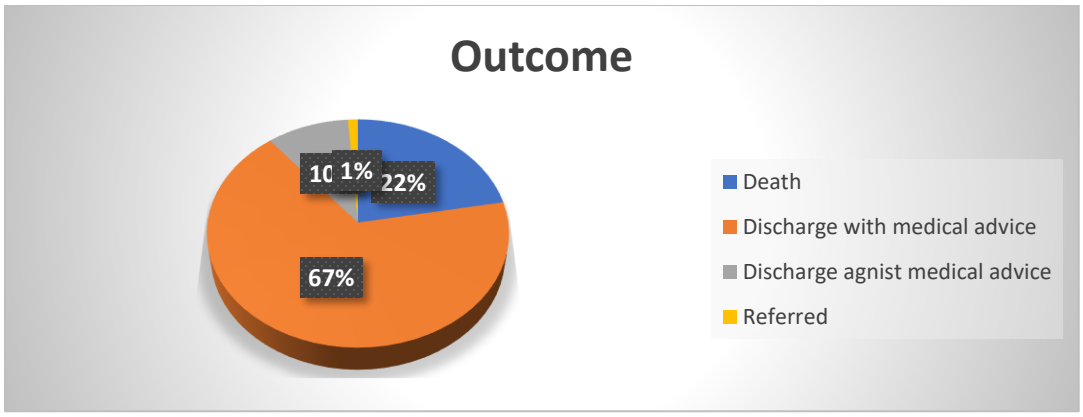

Figure 5: Outcome of adult stroke patients admitted in FHCSH, Northwest Ethiopia, January 2019 – November 2020

6.7 Time to death after admission

The median time was estimated using Kaplan Meier estimator. The median time to death was 19 days with IQR (10 days - unreachable).

Hazard function

As time goes, the probability of an individual survival due to stroke decreases after time t. The probability of stroke patient at time T which experience mortality shown below in figure 6.

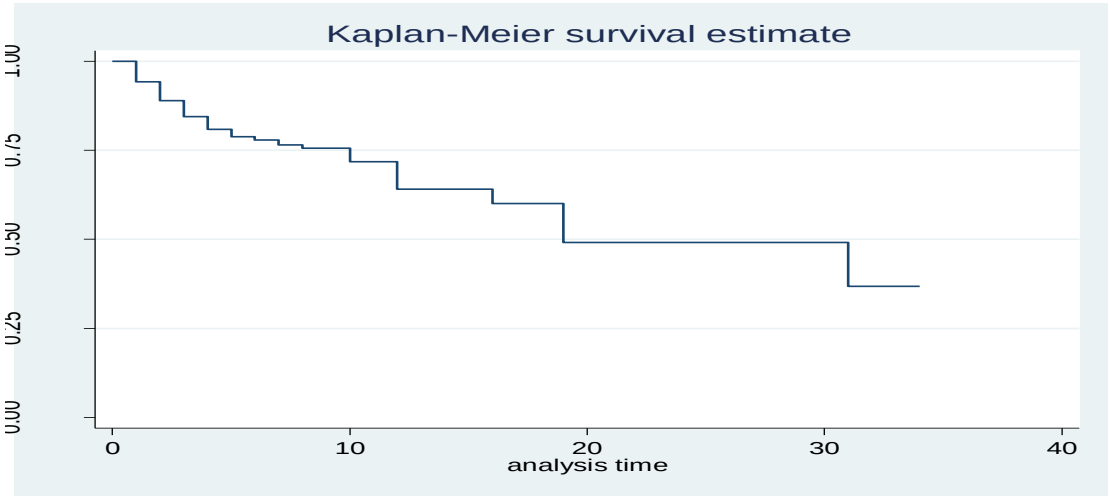

Figure 6: Kaplan-Meier survival graph of adult stroke patients admitted in FHCSH, Northwest Ethiopia, January 2019 – November 2020

PH assumption was checked by global goodness of test and the p-value was 0.49, which is statically non-significant (Table 6). Result of global goodness test for each variable, which included in the final model global can be found in Annex 4. In addition, time dependent of predictors was checked and covariates with time became non-significant (Annex 5).

Table 6: Global goodness of test for groups of predictors for data set of adult stroke patients admitted in FHCSH, Northwest Ethiopia, January 2019 – November 2020

	Chi square ($X^{2)}$	p-value
Global test	12.43	0.493

6.8 Predictors of Time to death

After the variables were screened using bivariate analysis with the p value < 0.2 as a cut of point, eleven (11) variables were entered into multi-variables cox regression model. The variables were sex, type of stroke identified, GCS, vomiting, ABM, urine incontinence, receiving anti-coagulant, receiving anti-platelet, AP, raised ICP, and time to hospital arrival.

Some variables (age and hypertension) which are clinically significant for stroke mortality, but their p-value were > 0.02, to check their statical relation to the outcome variable we included them in the final model. However, the variables became non-significant in the final model, and then we exclude them in the final report.

Cox proportional hazard model was used for the final analysis. On multivariable analysis, four variables were found to be significantly associated with the outcome, at the 95% CI. More specifically type of stroke identified (hemorrhagic), GCS (poor and moderate), AP (yes), and increased ICP (yes) were statistically significant predictors of time to death among admitted stroke patients (Table 7).

Table 7: Bivariate and adjusted predictors of death among adult stroke patients admitted in FHCSH, Northwest Ethiopia, January 2019 – November 2020

Variables	Categories	Survival status		CHR (CI)	p-value	AHR (CI)	p-value
		Death	Censored				
Sex	Male	42	194	1			
	Female	54	145	1.54 (1.02-2.3)	0.038	1	
Stroke type	Ischemic	45	249	1			
	Hemorrhagic	51	98	2.64 (1.77-3.96)	0.001**	1.8(1.03-3.3)	0.04
GCS during admission	Good	12	186	1		1	
	Moderate	29	119	3.03(1.55-5.95)	0.001	2.3 (1.03-4.2)	0.04
	Poor	55	34	11.9 (6.36-22.3)	0.001**	4.8 (2.35-9.83)	0.001**
Vomiting	No	68	282	1			
	Yes	28	57	0.56(0.36-0.88)	0.01		
Urine incontinence	No	69	292	1			
	Yes	27	47	0.59(0.37-0.92)	0.02		
ABM	No	84	329	1			
	Yes	12	10	0.3(0.19-0.66)	0.001		
Anti- platelets	No	42	98	1			
	Yes	54	241	1.7(1.16-2.62)	0.007		
Anti- coagulants	No	49	146	1			
	Yes	47	193	1.5 (0.99-2.2)	0.055		
AP	No	19	265	1		1	
	Yes	77	74	7.68 (4.64-12.73)	0.001**	3.5(1.9-6.1)	0.001**

ICP	No	72	329	1		1	
	Yes	24	10	5.2 (3.27-8.3)	0.001**	2.3 (1.34-3.9)	0.002*
Hospital arrival in hours	1-3	6	13	1			
	4-24	74	196	0.96 (0.42-2.22)	0.933		
	>24	16	130	0.34 (0.13-0.88)	0.026		

CHR- Crude hazard ratio, AHR- Adjusted hazard ratio, CI- Confidence interval, GCS – Glasgow Coma Scale, ABM-Abnormal body movement, ICP- Intra-cranial pressure, AP - Aspirated pneumonia, * - shows significant difference at $p<0.05$, ** - shows significant difference at $p<0.001$

7 Discussion

This study provided mortality rate, time to death and its predictors among stroke patients who were admitted to FHCSH. Out of 435 admitted stroke patients 96 of them died in the hospital.

The mortality rate among stroke patients were 22%. This result is lower than the study conducted in Burkina Faso (31). This discrepancy might be due to long hospital stay in Burkina Faso, which is the average stay is 12.1 days. Whereas, in the current study 5 days was the average hospital stay. When patients stay for many days in hospital, the risk of developing hospital acquired infection is high. Similarly, a study done in Bahir Dar Ethiopia, showed a mortality rate of 29.7% in stroke patients (28). This disparity may be due to the previous study follow up time included time after discharge, while our study was used only the admission period as follow up time. Studies conducted in Jimma and Brazil showed similar mortality rate with the current study (20) (29). In the contrary a study done in Gondar indicated low mortality rate (12.5%) than our study (7). This may be due to the later study used small sample size and reported only stroke mortality among ischemic stroke, ischemic stroke contribute less than half of the mortality reported by GBD of 2017, in our case both ischemic and hemorrhagic were included (12).

The median time of this study was 19 days, which is found to be longer when compared to a research done in Mekelle which was 3 days (25). The inconsistency may be due to in the previous study more than half (63%) of the participants were developed complication and this speed up the mortality of the patients. Also, a study done in Jimma reported shorter median time than our study (20).

After adjusting the other covariates, the hazard of early death among hemorrhagic stroke patients were 1.8 times more than the death of ischemic stroke patients. Studies done in Ethiopia, Zambia and Cameroon in line with our finding (22) (37) (43). However, a studies conducted in Uganda and Kenya shows stroke type is statistically non-significant (21) (44). This may be due to patients with hemorrhagic stroke have poor prognosis and half of the patients have risk of mortality.

In the current study, the hazard of early death among stroke patients with poor level of consciousness (GCS <8) were 4.2 times more than stroke patients with good level of consciousness (GCS 12-15) during admission. Also, stroke patients with moderate level of consciousness (GCS 8-11) had 2.08 times more early death than stroke patients with good level of consciousness (GCS 12-15) during admission. This result is consistence with studies conducted in Ethiopia, Uganda and Saudi Arabia (25) (41) (43) (44). This might be due to comatose patients or stroke patients with altered mental status have exposed to aspiration, brain edema and poor coma care (46).

In this study, the hazard rate of early death among stroke patients who developed AP were 2.9 times more than the death of stroke patients who had not developed AP. Studies done in Ethiopia, Sierra Leone and Zambia consistent with our finding (32) (37) (47) (34). This may be due to respiratory failure secondary to AP. In the contrary, a study done in Jimma, Ethiopia, provided that there is no statical difference on time of death among stroke patients who had developed Ap or had not developed AP (20).

This study found, the hazard of early death among stroke patients who had ICP was 2.4 times more than stroke patients who had not developed ICP. The current study in line with studies conducted in Ethiopia (20) (45) (34).

8 STRENGTH AND LIMITATIONS OF THE STUDY

8.1 Strengths

This study tried to estimate the median time of death and predictors among stroke patients (both ischemic and hemorrhagic stroke) during the admission period, which is done for first time in the study area. The study tries to include some behavioral factors to measure their effect on time to death among stroke patients. We had used large sample size. The cohort groups were also comparable in most of their baseline characteristics.

8.2 Limitations

Since the study was institutional based, the study was limited to adult stroke patients who present to the hospital, we cannot rule out potential selection bias (referral bias) for those who died out of hospital. The study used secondary data, and can't access information about some of sociodemographic factors (income) of the participant. By acknowledging these potential limitations, we hope that this finding can serve as baseline information for further research.

9 CONCLUSION AND RECOMMENDATIONS

9.1 Conclusions

We have found that the cumulative incidence rate of stroke death is 22%, which is higher than other previous studies. There was statistically significant difference in time to death among hemorrhagic and ischemic stroke patients. Type of stroke, Glasgow coma scale (GCS) at admission, stroke patients with raised ICP and aspirated pneumonia were the independent predictors of time to death among stroke patients.

9.2 Recommendations

Clinicians: We recommend clinicians to strengthen early identification and treatment of stroke complications along with strict follow up of comatose adult stroke patients and patients with hemorrhagic stroke, which can ultimately improve survival of stroke patients.

Researchers: We recommend researchers and scientific community to estimate the incidence of stroke death by doing a prospective study with large sample size which can measure personal behaviors that related to stroke

Policy makers: We recommend policy makers to design appropriate strategies for addressing the traditional modifiable risk factors of hemorrhagic stroke, and treatment and management of stroke complications. Designing treatment protocol regarding to stroke that could be used throughout the country

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10 Annex

Annex 1: Data abstraction checklist

Data abstraction checklist used for determining the time to death and predictors among stroke patients admitted in Felege Hiwot Comprehensive Specialized Hospital, Northwest Ethiopia: Retrospective cohort study.

Name of data abstractor: _____

Name of supervisor: _____

Date of data abstraction: _____/_____/_____

MRN: _____Checklist code: ___

Part 1: Socio-demographic characteristics

S.no	Variables	Category	S.no	Variables	Category
1.	Age (in years) ____		3.	Residence	1. Urban
2.	Sex	1. Male			2. Rural
		2. Female			

Part 2: Risk factors for stroke

S.no	Risk factors	Response
1.	Hypertension status	1. Yes 2. No
2.	Diabetes mellitus	1. Yes 2. No
3.	Cardiac illness	1. Yes 2. No
4.	Atrial fibrillation	1. Yes 2. No
5.	Previous history of stroke	1. Recurrent 2. New

Part 3: Behavioral factors

No	Variables	Responses
1	Smoking status	1. Yes 2. No
2.	Alcohol consumption	1. Yes 2. No

Part 4: Neurological factors

S.no	**Variables**	**Response**	**Remark**
1.	Type of stroke identified	1. Ischemic stroke 2. Hemorrhagic stroke	
2.	Clinical presentation at admission (Multiple responses are possible)	1. Altered mental status (Stupor/lethargy/coma) 2. Speech disturbances 3. Hemiparesis 4. Hemiplegia 5. Fascial palsy 6. Headache 7. Vomiting 8. Abnormal body movement	
3.	GCS score at admission	1. ≤8 (Unconscious) 2. 9-12 (Drowsy) 3. 13-15 (Alert)	

Part 5: Acute stroke events

S.no	**Variables**	**Responses**	**Remark**
1.	Vital signs on admission	1. BP (mmHg)_____ 2. PR (beats/min) _____ 3. RR (breaths/min) _____ 4. Temperature (^{o}c) _____	
2.	Date of stroke symptoms onset	_____/_____/_____(DD/MM/YY)	
3.	Date of hospital arrival	_____/_____/_____(DD/MM/YY)	
4.	Brain CT scan was done	1. Yes 2. No	
5.	Date of brain CT scan	_____/_____/_____(DD/MM/YY)	

6.	Other types imaging was done other than brain CT scan	1. Yes 2. No	If the answer is 2 skip Q7
7.	Types of imaging that was done	1. MRI 2. ECG 3. Chest X-ray	
8.	Type of treatment received (multiple responses are possible)	1. Antiplatelet (Aspirin, Clopidogrel) 2. Anti-coagulants (Heparin, Warfarin) 3. Ani-hypertensives 4. Statins 5. Anti-diabetic drugs 6. Antibiotics 7. Others (specify) _____	
9.	Stroke complications was detected	1. Yes 2. No	If the answer is 2 skip Q10
10.	If complication detects (Multiple responses are possible)	1. Aspiration pneumonia 2. Increased ICP 3. Seizure 4. Others (specify_____)	
11.	Treatment outcome	1. Dead 2. Censored	
12.	Date of death (if dead)	_____/_____/_____(DD/MM/YY)	If Q12 answered skip Q 13 & Q14
13.	Date of discharge (if alive)	_____/_____/_____(DD/MM/YY)	
14.	Way of discharge	1. With medical advice 2. Against medical advice 3. Referred	

Annex 2: Neurological factors of stroke patients

Table 8: Neurological factors of stroke patients admitted in FHCSH, Northwest Ethiopia, January 2019 – November 2020

Variables	Categories	Survival status		
		Death (%)	Censored (%)	Total frequency
Stroke type	Ischemic	45 (15.3)	249 (84.7)	294
	Hemorrhagic	51 (36.2)	98 (63.8)	141
GCS* during	Good	12 (6.1)	186 (93.9)	198
admission	Moderate	29 (19.6)	119 (80.4)	148
	Poor	55 (61.8)	34 (38.2)	89
Altered mental status	Yes	64 (54.2)	54 (45.8)	118
	No	32 (10.1)	285 (89.9)	317
Aphasia	Yes	69 (25.6)	201 (74.4)	270
	No	27 (16.4)	138 (83.6)	165
Hemiparesis	Yes	64 (18.2)	288 (81.8)	352
	No	32 (38.6)	51 (61.4)	83
Hemiplegia	Yes	7 (25.9)	20(74.1)	27
	No	89 (21.8)	319 (78.2)	408
Facial palsy	Yes	8 (13.8)	50 (86.1)	58
	No	88 (23.3)	289 (76.7)	377
Headache	Yes	19 (22.4)	66 (77.6)	85
	No	77 (22)	273 (78)	350
Vomiting	Yes	28 (32.9)	57 (67.1)	85
	No	68 (19.4)	282 (80.4)	350
Urine incontinence	Yes	27 (36.5)	47 (63.5)	74
	No	69 (19)	292 (81)	361
ABM*	Yes	12 (54.5)	10 (45.5)	22
	No	84 (20.3)	329 (79.7)	413

GCS* – Glasgow Coma Scale, ABM* - Abnormal body movement

Annex 3: Acute stroke presentation

Table 9: Acute stroke presentation of stroke patients admitted in FHCSH, Northwest Ethiopia, January 2019 – November 2020

Variables	**Categories**	**Survival status**		
		Death (%)	Censored (%)	Total frequency
SBP	90-139	39 (21)	147 (79)	186
	140-159	15 (16.4)	76 (83.6)	91
	≥160	42 (26.6)	116 (73.4)	158
DBP	60-89	39 (20.6)	150 (79.4)	189
	90-99	6 (18.2)	27 (81.8)	33
	≥100	41 (20.9)	155 (79.1)	196
Hospital arrival	1-3hr	6 (31.6)	13 (68.4)	19
	4-24hr	74 (27.4)	196 (72.6)	270
	>24hr	16 (11)	130 (89)	146
Way of diagnosis	Brain imaging	89 (22)	315 (78)	404
	Clinically	7 (22.6)	24 (77.4)	31
Complication	Yes	81(52.6)	73(47.4)	154
	No	15 (5.3)	266 (94.7)	281
AP	Yes	77 (51)	74 (49)	151
	No	19 (6.7)	265 (93.3)	284
ICP	Yes	24 (70.6)	10 (29.4)	34
	No	72 (18)	329 (82)	401
Seizure	Yes	2 (40)	3 (60)	5
	No	93 (21.6)	337 (78.4)	430

Annex 4: Global goodness of test

Table 10: Global goodness of test for groups of predictors for data set of adult stroke patients admitted in FHCSH, Northwest Ethiopia, January 2019 – November 2020

Variables	Categories	Survival status		X^2(df)	p-value
		Death (n)	Censored (n)		
Sex	Male	42	194	0.43(1)	0.512
	Female	54	145		
Stroke type	Ischemic	45	249	0.01(1)	0.916
	Hemorrhagic	51	98		
GCS during admission	Good	12	186	(2)	
	Moderate	29	119	0.25	0.610
	Poor	55	34	0.74	0.39
Vomiting	Yes	28	57	0.001(1)	0.968
	No	68	282		
Urine incontinence	Yes	27	47	0.02(1)	0.895
	No	69	292		
ABM	Yes	12	10	1.93(1)	0.164
	No	84	329		
Anti- platelet	Yes	54	241	0.31(1)	0.575
	No	42	98		
Anti- coagulants	Yes	47	193	0.42(1)	0.517
	No	49	146		
AP	Yes	77	74	1.35(1)	0.244
	No	19	265		

ICP	Yes	24	10		
	No	72	329	1.37(1)	0.242
Time of hospital arrival in hours	1-3	6	13	(2)	
	4-24	74	196	1.07	0.3
	>24	16	130	0.21	0.647
Global test				12.43	0.493

Annex 5: Test for Time dependent of predictors

Table 11: Test for time dependent of predictors for data set of adult stroke patients admitted in FHCSH, Northwest Ethiopia, January 2019 – November 2020

Variables	Categories	Survival status		p-value
		Death (n)	Censored (n)	
Sex	Male	42	194	
	Female	54	145	0.938
Stroke type	Ischemic	45	249	
	Hemorrhagic	51	98	0.821
GCS during admission	Good	12	186	
	Moderate	29	119	
	Poor	55	34	0.061
Vomiting	Yes	28	57	
	No	68	282	0.863
Urine incontinence	Yes	27	47	
	No	69	292	0.772
ABM	Yes	12	10	
	No	84	329	0.788
Anti- platelet	Yes	54	241	
	No	42	98	0.733
Anti- coagulants	Yes	47	193	
	No	49	146	0.406
AP	Yes	77	74	
	No	19	265	0.93
ICP	Yes	24	10	
	No	71	329	0.361
Time of hospital arrival in hours	1-3	6	13	
	4-24	74	196	
	>24	16	130	0.7