Clinical Characteristics and Outcomes of Acute ischemic stroke with Atrial fibrillation among patients admitted to Tertiary Care Hospitals in Amhara Regional State: Retrospective-cohort study

By: Zenaw Debasu (BPharm)

A Thesis Submitted to the Department of Pharmacology and Clinical Pharmacy, School of Pharmacy, College of Health Sciences, Addis Ababa University in Partial Fulfillment for the Requirements of the Degree of Master of Sciences in Pharmacy Practice

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Addis Ababa University

School of Graduate Studies

This is to certify that the thesis prepared by Zenaw Debasu Addisu, entitled: "***Clinical Characteristics and Outcomes of Acute ischemic stroke with Atrial Fibrillation among patients admitted to Tertiary Care Hospitals in Amhara Regional State: Retrospective-cohort Study***" and submitted in partial fulfillment of the requirements for the Degree of Master of Pharmacy in Pharmacy Practice complies with the regulations of the University and meets the accepted standards concerning originality and quality.

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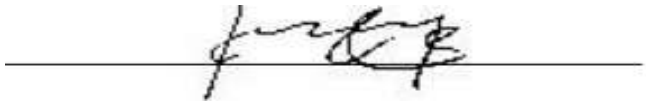
External Examiner: Kabaye Kumela (B. Pharm; MSc, Assistant Professor of Clinical Pharmacy) Signature:  Date: 6/20/2023

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Abbreviations/Acronyms

AF	Atrial fibrillation
AIS	Acute ischemic stroke
CT	Computed tomography
CKD	Chronic kidney disease
ECG	Electrocardiogram
GBD	Global Burden of Diseases
mRS	Modified Rankin Scale
NVAF	Non -valvular atrial fibrillation
NIHSS	National Institutes of Health Stroke Scale
RHD	Rheumatic heart disease
rt-PA	Recombinant tissue plasminogen activator
TIA	Transit ischemic attack
TOAST	Trial of Org 10172 in Acute Stroke Treatment
VAF	Valvular atrial fibrillation
WHO	World health organization

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Abstract

Background: Atrial fibrillation (AF) is commonly associated with cardioembolic stroke and is the major contributing factor to the increase in hospital expenditures for the care of stroke. However, evidence regarding clinical characteristics and outcomes of patients admitted with acute ischemic stroke (AIS) plus AF in Ethiopia is lacking.

Objective: To assess clinical characteristics and outcomes of acute ischemic stroke with atrial fibrillation among patients admitted to Tertiary Care Hospitals in Amhara regional state.

Methods: A retrospective cohort study was conducted among patients diagnosed with acute ischemic stroke and treated at Tibebe Ghion and Felege Hiwot CSHs from November 2018 - November 2021. Candidate patients were recruited using a consecutive sampling technique. Data were analyzed using SPSS version 25. Cox-regression analyses was used to identify the predictors of in-hospital mortality. The hazard ratio was used as a measure of the strength of the association and statistical significance was declared at p-value < 0.05. Besides, multivariate linear regression analysis was employed to explore predictors of length of hospital stay. The slope of regression line (β) with its 95% CI is used to declare statistical significance.

Result: Of the 378 patients with acute ischemic stroke, 58.7% were male. AF was diagnosed in 102 (26.9%) patients. Patients with AF were more likely to have Glasgow coma scale <8 (83.3 vs 4%, p< 0.001), valvular heart disease (56.9 vs 4.7 %, p< 0.001), and coronary heart disease (11.8 vs 4%, p=0.005). The incidence rate of in-hospital mortality was high for patients with atrial fibrillation (38 per 1000 person-days vs 17 per 1000 person-days). Glasgow coma scale < 8: (AHR=12.69, 95%CI: 2.603-61.873; p=0.002), Aspirational pneumonia (AHR=2.602, 95%CI: 1.085-6.242; p=0.032), Acute Renal Failure (AHR=6.114, 95%CI: 1.817, 20.576; p=0.003), Hypokalemia: (AHR=1.179, 95%CI: 1.112, 3.373; p=0.013), atrial fibrillation :(AHR=1.104, 95%CI: 1.015, 5.404; p=0.003), HIV/AIDS :(AHR=8.302, 95%CI: 1.585, 43.502 ; p=0.012) and Chronic liver disease :(AHR=4.969, 95%CI: 1.192-20.704 ; p=0.028) were the independent predictors of in-hospital mortality. Besides, deep vein thrombosis (β=7.337, 95%CI: 1.226,13.448; p=0.019), atrial fibrillation (β=1.696, 95%CI: 0.851,2.542; p=0.000), post-stroke depression (β=4.831, 95%CI: 2.330,7.332; p=0.000) and aspiration pneumonia (β=2.089, 95%CI: 1.178,3.000; p=0.000) were predictors of length of stay.

Conclusion: In this study, hospital mortality was higher in acute ischemic stroke associated with atrial fibrillation. Stroke-related complications were significant predictors of mortality and prolonged length of stay. Hence effective strategies should be in place to curb the impacts of these factors.

Keywords: Acute ischemic stroke, Atrial fibrillation, Clinical characteristics, Treatment outcome

1 Introduction

1.1 Background

Stroke is the second most common cause of mortality after ischemic heart disease and it accounts for 9% of fatalities worldwide [1].It also ranks as the fourth-largest global cause of disease burden [2]. World Health Organization (WHO) defines acute stroke as rapidly developing clinical signs of focal (or global) disturbances of cerebral function, with symptoms lasting 24 hours or longer or leading to death with no apparent cause other than of vascular origin [3]. Stroke makes an important contribution to morbidity, mortality, and disability in developed and developing countries. It leaves the patients with residual disabilities like physical dependence, cognitive decline, depression, and seizures [4].

According to the American Heart Association (AHA) report, stroke can be generally classified into either ischemic (87%) or hemorrhagic (13%) type [5]. Ischemic stroke, although significantly less fatal, has a 30-day mortality rate of 9% to 23% compared with 46.5% for hemorrhagic stroke [6]. Of these, approximately 25-40% are cardioembolic strokes attributable to atrial fibrillation[7].

Atrial fibrillation (AF) is the most common supraventricular tachyarrhythmia and the most common risk factor for ischemic stroke , mainly in the elderly [8]. It is also the most common arrhythmia that is associated with a high risk of stroke, particularly cardioembolic stroke [9]. The prevalence of stroke events due to AF has tripled over the recent 30 years. AF can be divided into the first detected episode, recurrent arrhythmia, paroxysmal, persistent, and permanent [10]. The guidelines recommend 24-hour Holter electrocardiogram (ECG) monitoring after acute ischemic stroke [11].

It has been reported that AF is one of the major contributing factors for hospital expenditures for the care of stroke [12]. AF independently increases the risk of ischemic stroke approximately 5-fold throughout all ages [13] and the prevalence increases steeply with age from 2% in patients younger than 50 years to 40% in those older than 90 years [14]. The common causes of atrial fibrillation are coronary artery disease, valvular heart disease, hypertension, sinoatrial disease,

hyperthyroidism, alcohol, cardiomyopathy, congenital heart disease, chest infection, pulmonary embolism, pericardial disease, idiopathic [15].

Because the overall burden of cardiovascular disease in developing nations is predicted to rise by about 150% over the next 20 years, due to an "epidemiological transition' from infectious diseases and nutritional deficiencies to more chronic disease conditions, subsequent success in the health care system depends on resolving this problem[16].

The burden of non-communicable diseases such as stroke and other cardiovascular diseases is increasing in Sub-Saharan Africa. Adding to the tropical diseases burden, it further strains the limited health care resources region [17]. According to WHO report of 2017, stroke deaths in Ethiopia reached 6.23% of total deaths. In addition, the age-adjusted death rate of stroke in the country is 89.82 per 100,000 of the population. Predominantly, ischemic stroke has been identified as the sixth leading cause of death [18].

Despite this, only few studies assessed stroke outcomes in Ethiopia [19, 20]. These studies reported that the prevalence of ischemic stroke is more common than hemorrhagic stroke and reported the overall mortality associated with stroke. The other hospital-based study by Greffie *et al*, reports that AF occurred in 27 (28.7%) of the cases. The prevalence of atrial fibrillation increased steeply with age. The study also shows AF was more common in patients with ischemic stroke than hemorrhagic stroke (34.8% vs 14.3%, P =0.049) [21].

1.2 Statement of the problem

The Global Burden of Diseases, Injuries, and Risk Factors (GBD) report on epidemiology of AF provide clear evidence of a long-suspected phenomenon of an increasing population of patients with AF [22]. This study estimated that in 2010, there were 33.5 million patients with AF in the world, constituting approximately 0.5% of the total world population. However, there appear to be significant differences in the developed and developing world related to mortality associated with AF.

The systematic review that included 72 published studies with a data generated from more than 20 sub-Saharan Africa reported that the prevalence of AF ranges from 6.7% to 34.8% in patients with ischemic stroke, 9.5% to 46.8% in those with rheumatic heart disease (RHD), and 5% to 31.5% in patients with dilated cardiomyopathy. The review also reports that community-based prevalence of AF was 4.3% and 0.7% in individuals aged ≥40 years and aged ≥70 years, respectively[23].

AF have bent to consume more resources which is one of the major contributory factors in hospital expenses including longer lengths of hospital stay and increased use of nursing care [24].

A cost-of-illness model study indicated that the total socioeconomic burden of AF-related stroke was high and accumulates on average 7–20% more costs than other strokes, with the majority being due to direct hospital and medical costs [25, 26]. Key contributors of the cost were reported informal care (i.e., made by family cares and self-help groups to coping patients with chronic illness), patients' productivity losses, and hospitalizations, accounting for more than half of the total costs of AF-related stroke events. Studies also report that AF-related stroke imposes a significant burden on healthcare systems and society [27].

According to the Danish Nationwide Registry-Based Cost of Illness Study from a Societal Perspective on First Acute Ischemic Stroke and Atrial Fibrillation, the estimated average societal cost of a stroke over the course of three years was $30,925 per patient, which is equal to $19,989 in the year that the stroke first occurred, $7,683 the following year, and $5,176 two years later. Over the course of three years, healthcare accounted for 66% of expenditure, whereas 26% and 8% of the costs were related to social care and lost productivity, respectively [28].

In Sub-Saharan Africa (SSA) the burden of stroke is on the rise owing to increasing incidences. There are young patients with stroke in SSA, resulting in a greater number of years of potential productivity and years of life lost (YLL)[29, 30]. This is also true in Ethiopia, the increasing burden of stroke in Ethiopia poses a challenge to the health care system [31]. Resources for stroke care and rehabilitation are scarce [32]. Indeed, patients with AF, increased the costs of acute hospitalization significantly. Discharge from a hospital to a residential or nursing facility in view of functional impairment and dependency, rather than the patient's home, can significantly increase the cost of post-hospital stroke care [25].

Studies suggested that stroke patients with AF have been shown to have a poorer neurological outcome than those without AF. A number of mechanisms have been proposed to explain this increased mortality among stroke patients with atrial fibrillation, including a higher stroke severity [33] higher age, [34] more comorbidity [35], and poorer quality of care [36]. However, the impact of these individual factors remains to be clarified.

Most of the current studies pertaining to the impact of AF on hospital outcomes has been limited by small numbers [15], with data generally obtained from a single hospital or community [9], especially in the older age groups [37]. Most study designs have primarily focused on the relationship between stroke risk factors and its outcome.

As far as our knowledge, there is only one published study in Ethiopia that assesses the prevalence of AF and its effect on outcome in stroke patients [21]. But the small sample size of the study reduced its power for drawing strong conclusion. The study did not asses the outcome of acute ischemic stroke (AIS) with AF. The study also involved only a single medical center hence, generalizing the findings may not be possible to the large population. Besides, there is limited information on characteristics, treatment, functional outcome, and case fatality of acute ischemic stroke with atrial fibrillation in Ethiopia. Therefore, this study was aimed to assess the clinical characteristics and treatment outcome of AIS with AF among hospitalized patients at Tibebe Ghion and Felege Hiwot Comprehensive Specialized Hospitals.

1.3 Significance of study

The result of this study will help to provide information regarding the clinical characteristic profile and treatment outcomes of AIS with AF. In-depth knowledge of the underlying clinical characteristic of AIS in patients with AF enable stakeholders (like health care providers, policymakers, governmental, non-governmental, and private organizations, trainers, and individuals involved in AIS with AF patients care) to develop strategies that can help to improve and choose the best method of in hospital treatment and outcome. This would in return help to improve the service provided to AIS with AF patients and hence improve survival. Furthermore, it will be used for other researchers as a reference source and it will also provide baseline information to conduct other similar studies.

2 Literature review

2.1 Clinical characteristics of AIS patient on admission

A retrospective cohort study that was conducted in China examining consecutive medical records of patients admitted within 72 hours of AIS symptom onset of patients with AIS. The study included 1,061 patients with acute ischemic stroke; 216 (20.3%) had AF. The incidence of bedridden state was 41.2% in patients with AF, compared with 23.7% in patients without. Other measures of clinical stroke severity showed similar differences between these groups. The odds ratio for bedridden Modified Rankin Scale (mRS) = 5 after ischemic stroke due to AF was 2.23 [38].

Similarly, a prospective cross-sectional study was conducted among patients with AIS admitted into the neuro-medicine and medical departments of Rajshahi Medical College Hospital, in Bangladesh. 125 patients with AIS participated in the study. 22 of the patients had AF. This study also revealed that 18 (81.8%) patients with AF were older than 45 years. Of the patients without atrial fibrillation, 95 (92.2%) were younger than 45 years. Of the patients with AF, 12 (54.4%) were male. In the group with AF, 1 (4.5%) was diagnosed with diabetes, 6 (27.3%) with hypertension, 5 (22.7%) with smoking, 2 (9.1%) with CKD, 3 (13.6%) with heart disease, and 3 (13.6%) with dyslipidemia. On admission, more severe disability was found in patients with AF (54.5% vs 51.5%) [15].

A hospital-based retrospective cohort study conducted in China involving 2,683 patients indicated that 366 (13.6%) of the patient were diagnosed with AF. In this patient, valvular AF accounted for 153 (41.8%) patients. Compared to patients without AF, patients with AF were found older (66.1 vs. 63.6) and had a higher national institutes of health stroke scale (NIHSS) score admission (median 10 vs. 4) and more frequently suffered from hemorrhagic transformation (7.3 vs. 2.8%, $p < 0.001$), pulmonary infection (27 vs. 10.6%), urinary tract infection (8.5 vs. 3.0%), acute gastrointestinal tract hemorrhage (4.1 vs. 1.9%), electrolyte disturbance (5.2 vs. 1.8%), acute renal failure (1.1 vs. 0.5) and urinary incontinence (3.8 vs. 0.6%) during hospitalization. The percentages of patients with AF who received oral anticoagulants were found 3.3% before stroke onset and 14.2% at discharge[9].

A prospective observational study in Malaysia that reviewed the multiethnic National Neurology Registry in Malaysian hospitals from July 29, 2009, to June 1, 2015, found that 311 (6.5%) of the 4762 ischemic stroke patients had AF. According to the study, there was no significant difference in the clinical presentation of symptoms between patients with and without AF. But, Patients with AF exhibited worse functional results (more impairment) and a higher proportion of stroke complications [39].

Multicenter survey in Europe involving 4462 hospitalized patients with first-ever strokes discovered AF in 803 patients (18.0%). AF patients were older, more typically female, and more likely to have had a previous myocardial infarction; they were less likely to be diabetics, alcohol drinkers, or smokers [40].

A prospective analysis of 172 ischemic stroke -AF patients conducted in Cameroon from 1 June 2006 to 30 June 2007 revealed that 75 were males and 97 were females, with a mean age of 65.8 +/- 13 years. Paroxysmal, chronic, and permanent AF were found in 22.7%, 21.5%, and 55.8% of people, respectively. Underlying cardiac problems were present in 156/172 patients (90.7%), including hypertensive heart disease (47.7%), valvular heart disease (25.6%), dilated cardiomyopathy (15.7%), and coronary artery disease (6%)[16].

A multicenter hospital-based registry in Italy included 3530 patients with AIS. The presence of AF at stroke onset and during the acute phase was found in 869 (24.6%) of 3530 patients with ischemic stroke. Compared with patients who did not have an arrhythmia, patients with AF were more often women and aged 80 years and older with coronary heart disease and peripheral arterial disease. 814 patients (93.7%) had chronic AF, while 55 (6.3%) had paroxysmal AF. Chronic AF was nonvalvular in 674 (82.8%) patients, valvular in 57 (7.0%), and unilateral or idiopathic in 83 (10.2%) [41] .

2.2 Treatment outcomes

A retrospective cohort study that involved 1688 patients with AIS at Bethesda Hospital in Yogyakarta, Indonesia, revealed that 45 (2.67%) of them had AF 51.11% of AF patients were men, and 82 .22% were older than 60. AIS patients with AF had a mortality rate of 18 (40.0%), and 37 (84.4%) had poor functional outcomes (mRs2) and a mean length of stay of 6(0-41) days. Compared to stroke patients without AF, patients with AF had significantly higher in-hospital mortality (RR: 2.11), worse disability (RR: 2.09), and longer hospital stays (6 (0-41 days) vs. 4 (0-14 days) [42].

Similarly, a population-based, prospective follow-up study in Denmark of 3,849 patients with AIS from Aarhus County that was registered between 2003 and 2007 found that, compared with patients without AF, patients with AF had a longer overall length of stay (median: 15 vs. 9 days) and had an increased risk of in-hospital medical complications (adjusted relative risk = 1.48) and recurrent stroke (adjusted hazard ratio = 1.30). The study also reported that the adjusted hazard ratios for 30 days mortality were 1.55 (95% CI: 1.20–2.01) in the AF group [43].

Hospital-based study retrospective cohort study conducted in China involving patients with AF reports that this group of patients had a higher proportion of disability determined as mRS score 3–5 in 3-month, 6-month, and 1-year follow-ups (46.6, 41.9, and 37.6 vs. 29.1, 24.0 and 19.3%, respectively) and had higher case fatality in hospitalization, 3-month, 6-month and 1-year follow-ups (10.1, 25.5, 29.1 and 34.0 vs. 2.0, 7.4, 8.8 and 11.6%, respectively) [9].

A retrospective analytical study involving 522,699 patients diagnosed with acute stroke and data retrieved from the Thailand national database found that 277,291 patients (53.1%) experienced an AIS. AF was present in 9.1% of patients who had an ischemic stroke. The death rates for acute ischemic stroke with AF were 14.1% whereas without AF was 6.2% [44].

A multicenter prospective hospital-based registration on patients with AIS in Japan from May 1999 to April 2000, reported that the AF group included 3335 (21.1%) patients (median age, 75 years), and the non-AF group included 12 496 (78.9%). Within 28 days of hospitalization, the mortality rate in the AF group was 11.3% and 3.4% in the non-AF group [45].

2.3 Predictors of mortality

A cross-sectional study, involved 74425 adults with AIS from the Austrian Stroke Unit Registry. The result reports that Stroke severity in general increased with age. AF was documented in 18962 (29,8), AF-related strokes were found more severe than strokes of other causes. Sex-related differences in stroke severity were only seen in stroke patients with AF. Median (Q25, 75) National Institutes of Health Stroke Scale score points were found 9 (4,17) in women and 6 (3,13) in men ($P<0.001$) [46].

A retrospective analytical study involving 522,699 patients diagnosed with acute stroke and data retrieved from the Thailand national database found that 277,291 patients (53.1%) experienced an AIS. AF was present in 9.1% of patients who had an ischemic stroke. The death rates for acute ischemic stroke with AF were 14.1% whereas without AF was 6.2%. Female gender (adjusted odds ratio; AOR 1.28), co-morbid disorders such as diabetes (AOR 1.28), hypertension (AOR 1.26), rt-PA medication (AOR 0.55), and stroke sequelae such as pneumonia (AOR 2.60), septicemia (AOR 6.50), or gastrointestinal bleeding were all significantly linked with mortality in acute stroke patients with AF (AOR 2.16)[44].

A consecutive cohort study was conducted involving 521 patients with AIS, the Netherlands Stroke Survey. A poor outcome (modified Rankin score > 2) was recorded at discharge. The result showed that stroke-associated infection was associated with poor outcomes at discharge [odds ratio (OR) 2.6, 95% confidence interval (CI) 1.0-6.7] [47].

A retrospective cohort study conducted in Taiwan involved 51 patients with pneumonia after acute ischemic stroke. Predictors of mortality were examined using univariate and multivariate analysis. The study found that a GCS score of < 9 on the day of onset of pneumonia was onset was the only significant predictor of mortality (hazard ratio, 6.72) [48].

A retrospective cohort study that included patients admitted to United States of America hospitals between 2002 and 2010 with acute ischemic stroke as their primary diagnosis and an Acute renal failure (ARF) as their secondary diagnosis was included in the data. The impact of ARF on rates

of intracerebral hemorrhage and discharge outcomes was examined. According to the findings, patients with AIS and ARF had a higher risk of death (odds ratio, 2.2) [49].

A retrospective cohort study involving 528 patients with AIS was carried out at a tertiary and teaching hospital at the University of Washington. Between October 2004 and December 2008, information was gathered from patient medical records from the time of admission to the hospital until discharge. the study reported that there was a higher in-hospital mortality rate from ischemic stroke (odds ratio [OR] 3.08) [50].

2.4 Predictors of length of hospital stay

A prospective cohort study that was carried out between January 1986 and December 2002 at the Sagrat Cor Hospital's department of neurology in Barcelona, Spain. In this study, a multiple regression model was used to examine the impact of various factors, including demographics, vascular risk factors, clinical, and neurological outcomes', on prolonged hospitalization. The dependent variable was a length of stay of 12 days or more (absent=0, present=1). The results of this study showed that 1536 (49.5%) of the 3112 acute stroke patients included in the study had a prolonged hospital stay. The longer length of stay was independently linked with male sex (OR = 1.16), limb weakness (OR = 1.79), vascular problems(included deep venous thrombosis and peripheral arterial embolism) (OR = 2.68), urinary complications (OR = 2.56), and infectious complications(Respiratory events included aspiration pneumonia, respiratory superinfection) (OR = 1,78); Nevertheless, symptom-free at discharge (OR = 0.45) and lacunar infarction (OR = 0.43) were inversely related to a prolonged hospital stay [51].

3 Objectives

3.1 General objective

- To assess clinical characteristics and outcomes of acute ischemic stroke with atrial fibrillation among patients admitted to Tibebe Ghion and Felege Hiwot Comprehensive Specialized Hospitals.

3.2 Specific objectives

- To assess clinical characteristics of acute ischemic stroke with atrial fibrillation
- Determine predictors of mortality among patients with acute ischemic stroke
- Identify predictors of length of hospital stay among patients with acute ischemic stroke

4 Method

4.1 Study area and period

The study was conducted at Tibebe Ghion Specialized Hospital (TGSH) and Felege Hiwot Comprehensive Specialized Hospital (FHCSH), two specialized referral public hospitals in Bahir Dar city, North-Western Ethiopia from November 2018 up to November 2021. Bahir Dar city is located 587 km northwest of Addis Ababa, the capital city of Ethiopia.

Tibebe-Ghion comprehensive specialized hospital was established in 2018. It is a teaching hospital under the college of medicine and health sciences of Bahir Dar University located in Bahir Dar, Ethiopia. The hospital provides a tertiary-level health care service and it is administered by Bahir Dar University. The hospital serves more than 5 million people in the catchment area and about 2000 patients per day in both inpatient and outpatient services. The hospital has more than 500 beds out of which 72 are reserved for medical adult patients.

Felege Hiwot comprehensive referral hospital was established in 1963. Felege Hiwot comprehensive referral hospital is a referral hospital located in Bahir Dar. It delivers health care services with medical, surgical, gynecological, orthopedic, intensive care units, pediatrics, and ophthalmological wards with a total of 400 beds capacity and around 15 adult outpatient departments and 561 staff. It serves a catchment population of more than 7 million, and about 500 clients visit the hospital daily. The internal medicine ward contains 85 beds.

4.2 Study design

A retrospective cohort study was employed.

4.3 Population

4.3.1 Source population

The source population was all adult patients admitted to the medical wards with the diagnosis of stroke based on the WHO's clinical case definition.

4.3.2 Study population

The study population was all acute ischemic stroke with atrial fibrillation patients admitted to the medical ward at Tibebe Ghion comprehensive Specialized Hospital and Felege Hiwot Comprehensive Specialized Hospital between November 2018 till November 2021 and fulfilled the inclusion criteria were consecutively enrolled in this study.

Those patients with acute ischemic stroke and atrial fibrillation (AIS plus AF) were included in the exposed cohort and those patients with acute ischemic stroke only (AIS alone) were included in the non-exposed cohort.

4.4 Eligibility criteria

4.4.1 Inclusion criteria

- Age ≥ 18 years
- Acute ischemic stroke diagnosed according to the WHO Guideline for Diagnosis and Treatment of acute ischemic stroke.
- Patient with a history of persistent AF or paroxysmal AF, supported by past electrocardiogram (ECG) or diagnosed by the attending physicians based on ECG and/or 24-hour ECG monitoring during admission.

4.4.2 Exclusion criteria

- Patients with cerebral hemorrhage confirmed by CT imaging or MRI
- Patients with TIA
- Patients with incomplete medical records

- Missing AIS patient charts
- Patients with an unknown discharge status

4.5 Sample size determination and allocation

The sample size for this study was calculated with Epi info 7.25 software using a 19 % probability of death among patients with acute ischemic stroke and atrial fibrillation and 10% among patients with acute ischemic stroke only in another similar setting [52], 80% power, and 2:1 ratio, of unexposed to exposed, and 5% significance level. Accordingly, the final sample size computed based on the above assumption is 475 which comprises 190 patients for acute ischemic stroke with atrial fibrillation and 285 patients for acute ischemic stroke only. However, due to limited number of admissions, the study included all samples that met inclusion criteria during the study period. So, the data of 378 patients (102 patients from acute ischemic stroke with atrial fibrillation and 276 patients from acute ischemic stroke only) were found.

4.6 Study variables

4.6.1 Independent variables

- Sociodemographic factors
  - Age
  - Sex
  - Marital status
- Disease-related factors and co-morbidities
  - Hypertension
  - Diabetes mellitus
  - Hyperlipidemia
  - Coronary heart disease
  - Myocardial infarction
  - HIV/AIDS
- Clinical presentation on admission
- Glasgow Coma Scale (GCS)
- Time of hospital admission after ischemic stroke onset
- Stroke-related complications during hospitalization (hospital stay)
  - Pulmonary infection
  - Urinary tract infection

- Intestinal infection
- Acute gastrointestinal tract hemorrhage
- Electrolyte disturbance
- Bedsore
- Acute renal failure
- Urinary incontinence
- Pulmonary embolism
- Hemorrhagic transformation

- Medication-related factors (Dosage regimen, type, and a class of medications of previous medication
  - Thrombolysis
  - Antiplatelets
  - Anticoagulants
  - Antihypertensives
  - Statins
  - Antidiabetic drugs

4.6.2 Dependent variables

- Treatment outcomes
  - Primary outcome: In -hospital mortality
  - Secondary outcome: Length of hospital stays

4.7 Data collection instrument and procedure

The records of acute ischemic stroke patients admitted at Tibebe Ghion comprehensive Specialized Hospital and Felege Hiwot Comprehensive Specialized Hospital three-year period (November 2018- November 2021) were reviewed using an English version checklist. The checklist was prepared after reviewing different relevant literature and the charts of patients who fulfilled the WHO's clinical case definition of ischemic stroke. The investigators and trained data collectors; two nurses and two pharmacists collected all relevant data including socio-demographics, risk factor profile, clinical presentation, medication used for treatment, treatment outcomes, and prophylaxis, presence of atrial fibrillation, and subtype from the case records using structure data extraction form.

4.8 Statistical analysis

Data analyses were performed using the statistical package for social sciences (SPSS) version 25. Descriptive analysis was performed and results were presented in text, tables, and charts. Continuous variables were reported using mean, median, and interquartile ranges. A chi-square test was performed to check the differences in baseline characteristics. Multivariate Cox regression was performed to identify independent predictors of in-hospital mortality. Bivariate Cox regression was performed to pick variables for multivariable Cox regression. Variables with p-value < 0.2 in bivariate regression were considered for multivariable Cox regression. Kaplan Meier analyses were used to identify the survival rates and median survival time. The hazard ratio was used as a measure of the strength of the association and a p-value < 0.05 was considered to declare statistical significance at a 95% confidence interval. Bivariate and multivariate linear regressions were also carried out to assess independent predictors of LOS. Bivariate linear regression was performed to identify candidate variables for multivariable linear regression. Variables with a p-value ≤ 0.2 in bivariate regression were candidates for multivariable regression. Multivariable linear regression was performed using the backward method to identify independent predictors. Regression coefficients and their 95% confidence intervals together with p-value < 0.05 were used to identify independent predictors. In order to address possible problems with collinearity, the tolerance and the variance inflation factor (VIF) values of each independent variable were assessed.

4.9 Data quality management

The principal investigator provided training to data collectors in order to build a shared understanding of how to collect data and familiarize them with the data extraction checklist. The principal investigator provided on-site supervision and feedback to data collectors on a daily basis. The validity and reliability of the instrument were tested on 5% of the total sample size at Debremarkos comprehensive specialized hospital before the actual data collection time. The data collection format was cross-matched with accessible information on records before beginning data collection, and the study questions were rearranged as necessary. The incomplete chart was discarded. Clarity and consistency were checked on all completed data-collecting forms. The data

was reviewed regularly for consistency, completeness, clarity, and accuracy. Any errors, doubts, or incompleteness were addressed appropriately.

4.10 Ethical considerations

The ethical approval and clearance were obtained from the Ethics Review Committee of the School of Pharmacy, College of Health Sciences; Addis Ababa University through a letter reference number of ERB/SOP/489/15/2022. This study required secondary data from medical case records based on the routine procedures of the hospitals, being secondary data, it is difficult to assure informed and written consent from the patients so permission was secured from each hospital's quality assurance department. The privacy of personal information was strictly preserved. The data from the case records were handled with strong confidentiality. Neither the case records nor the data extracted were used for any other purpose.

4.11 Operational definition

- **Ischemic stroke**: patients who fulfilled the WHO's case definition of stroke had brain CT scan results and standard 12 lead ECG report.
- **Acute ischemic stroke:** is ischemic stroke with symptom onset-to-arrival time within 24 hours to seven days [53]
- **Atrial Fibrillation**: The diagnosis of atrial fibrillation is made by reviewing the attached 12 lead ECG strips if available or if an ECG reading report with index of AF was found in the case records.
- **Glasgow Coma Scale (GCS)** is defined as good if the patient has mild brain injury/alert, GCS (13-15) or moderate brain injury/drowsy, GCS (9-12). GCS is defined as poor if the patients had severe brain injury/unconscious, GCS (≤ 8) [54].
- **Treatment outcome**: in this study, treatment outcome refers to the status of patients during hospital discharge (in-hospital mortality) upon in-hospital treatment and the length of hospital stay. In-hospital treatment includes all treatment given by the stroke team as soon as the patient arrives at the hospital, patient management according to national standard

treatment guidelines, anticoagulation, pharmacotherapy for risk factors, treatment to provide to prevent complications, and treatments that provided specific care.

- **Survival status**: The status of the patient's survival to the outcome (death) or censored.
- **Censored**: Time to event is not observed for reasons such as the subject had left against medical recommendation prior to experiencing an event.
- **Time to death**: was the time between the date of diagnosis of AIS and the date of in-hospital death.
- **Length of hospital stay**: was defined as the amount of time between hospital admission and discharge. Admission date was defined as the date the patient was admitted to the hospital with acute ischemic stroke or if the patient was already in the hospital for another condition, the day the stroke actually occurred. The date that a patient is transferred from the stroke unit to their home, another hospital, or a rehabilitation facility is referred to as the discharge date.

4.12 Plan for dissemination of study result

The finding of this study will be disseminated to the Addis Ababa University College of Medicine and Health Sciences School of pharmacy, to Tibebe Ghion and Felege Hiwot Comprehensive Specialized Hospitals and Amhara regional health bureau, and to other stroke coordinating organizations to improve hospital treatment acute ischemic stroke with atrial fibrillation. Furthermore, the findings will be presented at national and international scientific conferences, as well as published in a reputable journal.

5 Results

Between November 2018 and November 2021, 470 patients with ischemic stroke were enrolled at two hospitals in the region. Among the 470 eligible patients' charts, 92 patients' charts were eliminated for a variety of reasons. Therefore 378 (AIS with AF = 102, AIS alone = 276) patients were included in the final analysis fig (1).

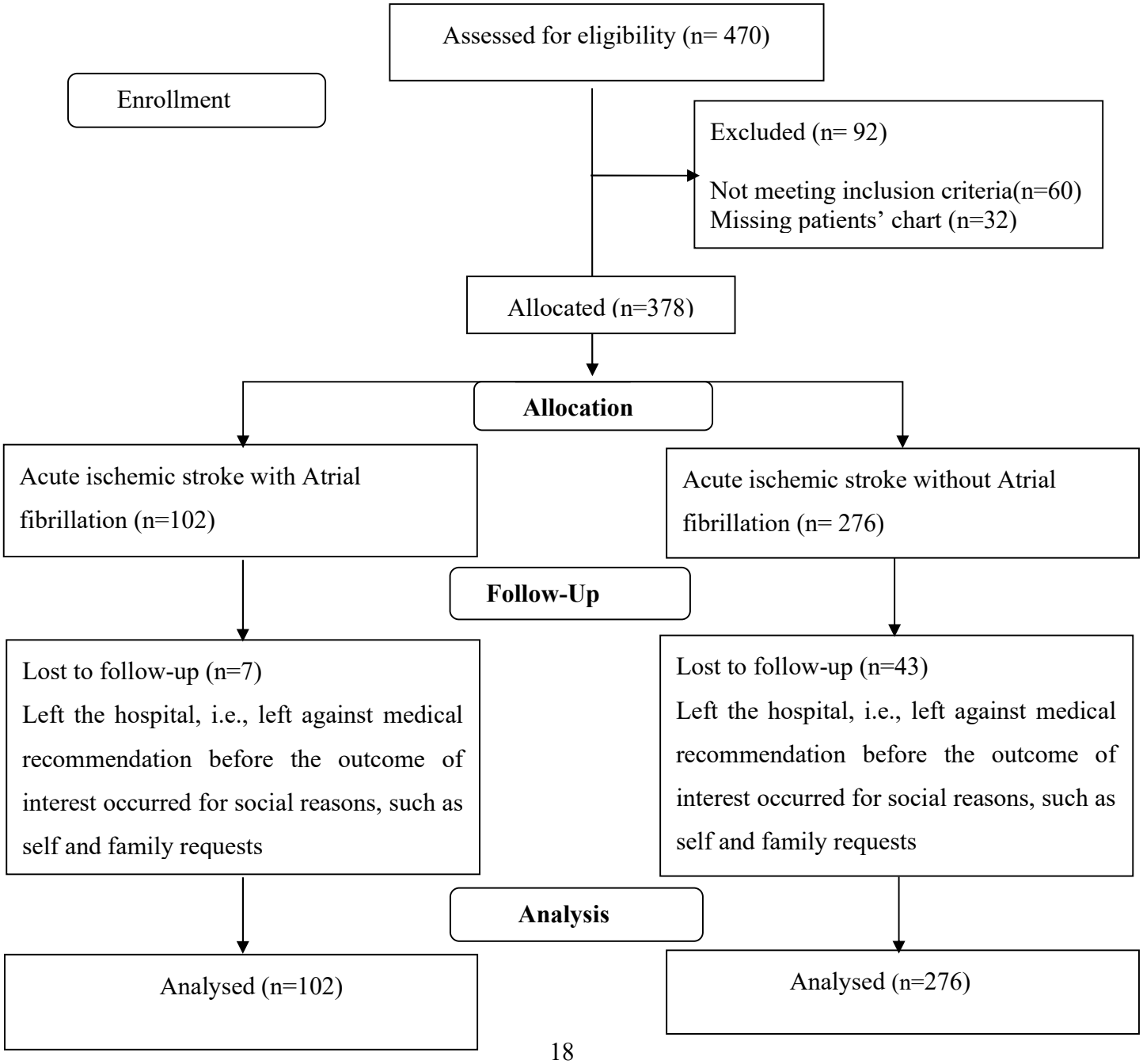

Figure 1 :Flow chart showing a selection of patients with diagnose with AIS from FHSCH and TGSCH from November 2018 to November 2021

Majority of patients 223 (59%) were from Felege Hiwot comprehensive Specialized Hospital and 155 (41%) were from Tibebe Ghion Comprehensive Specialized Hospital.

5.1 Socio-demographic characteristics

Of the 378 eligible patients' charts, more than half, 222 (58.7%) of the patients were male and 244 (64.55%) were rural residents. Besides 274 (72.5 %) were married while 81 (21.7%) were widowed. The majority, 204 (54 %) of patients were farmers followed by 55 (14.6%) unemployed. Regarding religion, 317 (83.9%) were Orthodox Christians. Of the total patients, 264 (69.8%) had no formal education (Table 1).

Table 1: Socio-demographic characteristics of patients diagnose with AIS from FHSCH and TGSCH from November 2018 to November 2021 (n=378)

Socio-demographic characteristic		AIS plus AF (102)	AIS alone (276)	Total 378 (%)
Sex	Male	48 (47.1%)	174 (63%)	222 (58.7%)
	Female	54 (52.9%)	102 (37%)	156 (41.3%)
Age	<= 53	19(18.6%)	60 (21%)	79 (20.9%)
	54-64	11 (10.8%)	61 (22.1%)	72 (19%)
	65-74	35 (34.3%)	83 (30.1%)	118 (31.2%)
	75-84	28 (27.5%)	64 (23.2%)	92 (24.3%)
	>=85	9 (8.8%)	8 (2.9%)	17 (4.5%)
Marital status	Single	7 (6.9%)	5(1.8%)	12 (3.2%)
	Married	66 (64.7%)	208(75.4%)	274 (72.5%)
	Divorced	1 (1%)	10 (3.6%)	11 (2.9%)
	Widow	28 (27.5%)	53(19.2%)	81 (21.4%)
Residency	Urban	43(42.2%)	91(33%)	134 (35.4%)

	Rural	59(57.8%)	185(67%)	244 (64.6%)
Religion	Orthodox	82 (80.4%0	235 (85.1%)	317 (72.5%)
	Protestant	13 (12.7%)	24 (8.7%)	37 (9.8%)
	Muslim	7 (6.9%)	15 (5.4%)	22 (5.8%)
	Catholic	0 (0.0%)	2 (0.7%)	2 (0.5%)
Educational status	No formal education	69 (67.6%)	195 (70.7)	264 (69.8%)
	Primary school (1-8)	7 (6.7%)	31 (11.2%)	38 (10.1%)
	Secondary school (9-12)	12 (11.8%)	23 (8.3%)	35 (9.3%)
	Collage /university	14 (13.7%)	27 (9.8%)	41 (10.8%)
Employment level	Employed	13 (12.7%)	26 (9.4%)	39 (10.3%)
	Farmer	47 (46.1%)	157 (56.9%)	204 (54%)
	Unemployed	20 (19.6%)	35 (12.7%)	55 (14.6%)
	Housewife	17(16.7%)	30 (10.9%)	47 (12.4%)
	Self-employed	5 (4.9%)	28 (10.1%)	33 (8.7%)

5.2 Baseline characteristics of the study participants

Of the 378 patients admitted with AIS, 102 (26.9%) were diagnosed with AF. This group consisted of 58 (56.9%) valvular atrial fibrillation (VAF) patients, and 44 (43.1%) non-valvular atrial fibrillation (NVAF) patients. Table 2 demonstrates the baseline characteristics of AIS patients with and without AF during hospital admission. According to Trial of Org 10172 in Acute Stroke Treatment (TOAST) criteria, 95 patients in the AF group were diagnosed as cardioembolic, accounting for 93.1% (95/102) of the patients and the remaining were categorized as strokes of undetermined etiology.

Female patient with AIS had a greater and considerably higher frequency of AF (52.9 vs 47.1%, P=0.005). AIS plus AF was significantly higher frequency in all age groups except those under the age of 53 and those between the ages of 54 and 64. Patients in the AIS plus AF group were a considerably higher frequency of a GCS of less than 8 (85 (83.3%) versus 11 (4%)), but mild and

severe brain damage were significantly higher frequency in the AIS alone group, i.e., mild brain injuries (2 (2%) vs. 184 (66.6%)) and for moderate brain injuries (15(14.7%) vs 81 (29.3%)) respectively.

Regarding comorbidity, patients with AIS Plus AF had a significantly higher frequency of valvular heart disease (i.e., CRVHD, prosthetic heart valve, mechanical heart valve) (58 (56.9%) vs. 13 (4.7%)), CHD (12 (11.8%) vs. 11 (4%)), and DCMP (9 (8.8%) vs. 8 (2.9%)) and a significantly lower frequency of Hypertensive status. Moreover, there is no significant difference in time from symptom onset to hospital, alcohol consumption, and HHD, between groups. Although smoking was significantly higher in a patient with AIS plus AF, hyperlipidemia and current alcohol consumption were more common among patients with AIS alone. Only 17 (16%) of the AF group received oral anticoagulants prior to stroke onset, and 10 of these patients had an international normalized ratio (INR) on the admission of less than 2.

Table 2: Baseline characteristics of acute ischemic stroke patients with atrial fibrillation and those without atrial fibrillation (n=378)

Variables	Category	ECG finding		Chi-square p-value
		AIS plus AF	AIS alone	
Sex	Female	54 (52.9%)	102(37%)	0.005
Mean age		65.75 ±16.4	63.5±13.58	0.022
Age	< 54	19(18.6%)	60(21.7%)	0.016
	54-64	11 (10.8)	61 (22.1%)	
	65-74	35 (34.3)	83 (30.1%)	
	75-84	28 (27.3%)	64 (23.2%)	
	>85	9 (8.8%)	8 (2.9%)	
Time from symptom onset to hospital	<= 3 hours	3 (2.9%)	10 (3.6%)	0.747
	>3 hours	99 (97.1%)	266 (96.4%)	
LDL level	LDL<100	62 (23.2%)	16 (20.3%)	0.037
	LDL >=100 mg/dl	126(66.7%)	63(79.7%)	

Hypertensive status	Newly diagnosed HTN	7 (6.9%)	40 (14.5%)	0.027
	Known hypertensive patient	40 (39.2%)	124 (45.1 %)	
Alcohol	Current alcohol use	20 (21.1%)	83 (32.3%)	0.053
	Former drinker	16(16.8%)	26 (10.1%)	
GCS	Mild (13–15))	2(2%)	184(66.6%)	0.000
	Moderate (9–12)	15(14.7%)	81(29.3%)	
	Severe (<8)	85(83.3%)	11(4%)	
Comorbidity	VHD	58(56.9%)	13 (4.7%)	0.000
	HHD	12(11.8%)	21 (7.6%)	0.204
	CHD	12 (11.8%)	11 (4%)	0.005
	DCMP	9(8.8%)	8(2.9%)	0.014

Key: LDL: low-density lipoprotein, GCS: Glasco coma scale, *VHD: Valvular Heart Disease, HHD: Hypertensive heart disease, CHD: Coronary heart disease, DCMP: Dilated cardiomyopathy, AIS: acute ischemic stroke, AF: atrial fibrillation*

5.2.1 Neurologic deficits during admission of acute ischemic stroke patients with and without atrial fibrillation

Table 3 compares the clinical presentation of neurologic deficits at admission in patients with AIS plus AF and AIS alone. The most common neurological deficit during hospital admission in the AF group was right or left side body weakness 99 (97.1%) followed by Aphasia 86 (84.3%), loss of consciousness 69 (67.6%), and facial palsy 61(59.8%) similarly most non-AF group presented with right or left side body weakness 99 (97.1%) followed Aphasia 249 (90.2%), Hemiparesis, 125 (45.3%) and loss of consciousness 116 (42.0%).

Table 3 Comparison of neurologic deficits during admission among patients with acute ischemic stroke patients plus atrial fibrillation and those without atrial fibrillation

Neurologic deficits during admission	AIS plus AF	AIS alone	Total
LOC	69 (67.6%)	116 (42.0%)	185
Hemiparesis	44(43.1%)	125(45.3%)	169
Aphasia	86 (84.3%)	249(90.2%)	335
facial palsy	61(59.8%)	144(52.2%)	205
Weakness	99 (97.1%)	268(97.1%)	367
Urinary incontinence	26 (25.5%)	68 (24.6%)	94
Headache	41(40.2%)	118(42.8%)	159
Convulsions/ABM	11 (10.8%)	24(8.7%)	35
Swallowing difficulty/dysphagia	0(0.0%)	5(1.8%)	5
loss of memory	0(0.0%)	1(0.4%0	1
Loss of vision	0(0.0%)	2(0.7%)	2
Bilateral hearing loss	0(0.0%)	1(0.4%)	1
Neck stiffness	0(0.0%)	1(0.4%)	1

Key: LOC: Loss of consciousness, ABM: Abnormal body movement,

5.2.2 In-hospital treatment prescribed to the study participants

Regarding medications prescribed during hospitalization patients with AF had received a higher frequency of statin 101 (99%) followed by antiplatelet 95 (93.1%), antithrombotic 77 (75.5%), antibiotics 42 (41.2%), and only 39(38.2%) patients were prescribed with anticoagulants. Other common prescribing medications like anticonvulsants (3(2.9%)), potassium chloride supplements (7(6.9%)), and diuretics (1(1%)) are less frequently prescribed in a patient with AIS plus AF. Among patients without AF antiplatelet 270 (98.2%), were prescribed more frequently followed by statin 271 (98.5%), antithrombotic 180 (65.5%), antibiotics 73 (26.5%), and antihypertensive 87(31.6%) as shown in Table 4.

Table 4: In-hospital treatment prescribed of patients with acute ischemic stroke plus atrial fibrillation and without atrial fibrillation

In hospital treatment	AIS plus AF	AIS alone	Total
Antiplatelet	95 (93.1%)	270 (98.2%)	365
Anticoagulant	39(38.2)	12 (4.4%)	51
Antihypertensive agents	22(21.6%)	87(31.6%)	109
Statins	101 (99%)	271 (98.5%)	372
Antidiabetic agents	6(5.9%)	11 (4%)	17
Antithrombotic	77 (75.5)	180(65.5%)	257
Ventricular rate controls	30 (29.4%)	2 (0.7%)	32
Antibiotics	42 (41.2%)	73 (26.5%)	115
Anticonvulsant	3 (2.9%)	12 (4.4%)	15
Potassium chloride supplement	7(6.9%)	10(3.6%)	17
Diuretics/osmotic agents	1(1%)	11(4%)	12
Antidepressants	0(0%)	3(1.1%)	3

5.2.3 In-hospital complications among the study participants

Acute renal failure (22.5% vs 3.3%), hypokalemia (18.6% vs 10.1%), Aspirational pneumonia (42.2% vs 28.7%), and Hemorrhagic transformation (11.8% vs 4.3%) are considerably more likely in-hospital complication in AF groups than non-AF groups respectively. Although the difference is not statistically significant, the frequency of urinary tract infection, urine incontinence, and increase in intracranial pressure is higher in the groups without AF. Table 5 shows complications that occur in hospitals.

Table 5: Stroke-related complications during hospital stay in a patient with acute ischemic stroke plus atrial fibrillation and without atrial fibrillation

Variables	AIS plus AF	AIS alone	Chi-square p-value
Aspirational pneumonia	43(42.2%)	79(28.7%)	0.013
Urinary tract infection	4(3.9%)	12(4.3%)	0.855

Urinary incontinence	2(2.4%)	7(3.7%)	0.571
Acute renal failure	23(22.5%)	9(3.3%)	0000
Hypokalemia	19(18.6%)	28(10.1%)	0.027
Acute gastrointestinal hemorrhage	3(2.8%)	5(1.8%)	0.498
Hemorrhagic transformation	12(11.8%)	12(4.3%)	0.009
Pulmonary embolism	2(2%)	0	NA
Post-stroke depression	2(2%)	4(1.4%)	0.724
Increase intracranial pressure	0	6.(6%)	0.133
Hospital-acquired pneumonia	1(1%)	6(2.2)	0.445
Deep venous thrombosis	1(1%)	3(1.1%)	0.928
Bedsore	1(1%)	4(1.4%)	0.723
In-hospital death	26(25.5%)	24(8.7%)	0.000

5.3 Treatment outcome of the study participants

About 59% (61) of patients from the AIS plus AF group and 68.8% (190) patients from the non-AF group were discharged with improvement. Eight (7.8%) patients from AIS plus AF group and 19(6.88%) patients from the AIS alone group were discharged without improvement. Due to various social reasons, such as self and family requests, 7 (6.66%) patients from the AIS plus AF group and 43 (15.5%) patients from the AIS alone group were discharged against medical recommendation. According to our findings, the rate of in-hospital mortality due to acute ischemic stroke was 13.22%. Among these, 26 (25.5%) patients were from the AF group and 24 (8.7%) patients were from the AIS alone group.

The in-hospital mortality rate of acute ischemic stroke patients with AF was 25 per 100, while those without AF were 8.7 per 100. The incidence rate of mortality for acute ischemic stroke with atrial fibrillation was 38 per 1000 person-day. For survival analysis, all patients that met inclusion criteria and patients who had started in-hospital treatment were included in the analysis .The in-hospital survival rate was 30.2% with a mean survival time was 12.75 days (95% CI: 11.241 - 14.268). The estimated cumulated survival rate of AIS-with AF patients at the 1st, 7th, 10th, 14th,

and 15th days was 93.1%,75.4%,66.9%,54.4%, and 45.3% respectively. The probability of survival was highest on the first day of admission, but it was shortened as follow-up time increased. On the other hand, the incidence rate of mortality for acute ischemic stroke without atrial fibrillation was 17 per 1000 person-day. The in-hospital survival rate was 52.8 % with a mean survival time was 15 days (95% CI: 13.523 -16.59). Kaplan-Meier analysis with the log-rank test evaluated in-hospital survival rate for patients with AF compared to patients without AF was significantly different (P=0.011 fig.2). The median follow-up time for this cohort was 5.49 (±3.575) days, which ranged from 1 day to a maximum of 19 days.

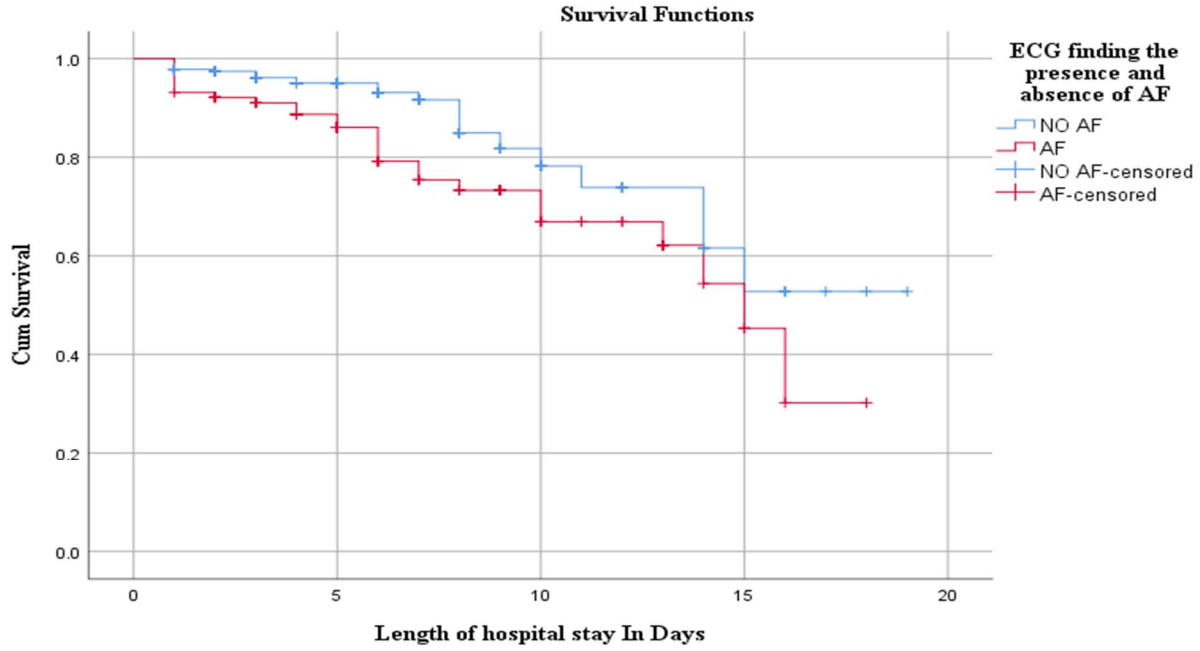

Figure 2 : Kaplan-Meier estimation of survival rates in patients with AF and patients without AF

As documented on the death certificate, the most common causes of death in the AF group were respiratory failure related to aspirational pneumonia (9), AF itself (4), brain herniation (3), hemorrhagic transformation (2), multiorgan failure (2) and cardiogenic shock (2).

5.4 Predictors of in hospital mortality

A bivariate cox regression analysis was performed to assess the predictors of in-hospital mortality. Variables that were significant at p <0.2 level in the bivariate cox regression model were the presence of AF, Cardiovascular diseases such as DCMP, Chronic liver disease, HIV/AIDS, stroke-related complications such as aspirational pneumonia, acute renal failure, hypokalemia and hemorrhagic transformation, comorbidities such as hyperlipidemic status during admission, and hypertension status of the patient associated with in-hospital mortality, and they were candidates for multivariable cox regression. Table 6

Accordingly, a multivariable cox-regression analysis found that Glasgow Coma Scale (GCS) less than 8 i.e., Severe brain injury (unconscious) during hospital admission increased the hazard of death by 12.6 times (AHR=12.69, 95%CI: 2.603-61.873) compared to patients who had had GCS of 9-12. Besides, those Patients with chronic liver disease during hospitalization had a nearly 5-fold higher risk of in-hospital mortality (AHR=4.969, 95%CI: 1.192-20.704). Similarly, the presence of comorbid HIV/AIDS increased the hazard of death by 8.302 times (AHR=8.302, 95%CI: 1.585, 43.502). In addition, Patients who acquired Stroke-related complications of Aspirational pneumonia during hospitalization or hospital stay had a 2.6 times higher risk of in-hospital mortality (AHR=2.602, 95%CI: 1.085-6.242). Besides, Patients who developed Acute Renal Failure during hospitalization or hospital stay were 6.114 times more likely to die during the hospital stay (AHR=6.114, 95%CI: 1.817, 20.576). Whereas, patients who developed develop Hypokalemia during hospitalization or hospital stay by 17.9% increased the hazard of in-hospital mortality (AHR=1.179, 95%CI: 1.112, 3.373). Moreover, the presence of atrial fibrillation during hospitalization or hospital stays increased hospital mortality by 10.4% (AHR=1.104, 95%CI: 1.015, 5.404).

Table 6: Bivariate and multivariate cox-regression analysis result to predictors contributing to survival of acute ischemic stroke patients with atrial fibrillation and those without atrial fibrillation. (n=378)

Variables		Patient status		CHR (95% CI)	P value	AHR (95% CI)	P value
		died	Alive				
Hypertension status	No hypertensive comorbidity	25	141				
	Newly diagnosed	2	45	0.211 (0.05,0.895)	0.108	0.226(.027, 1.935)	0.175
	Known hypertensive patient	23	141	0.906 (0.514,1.599)	0.735	1.293 (0.526, 3.177	0.575
LDL level	Lipid controlled (LDL<100)	6	72				
	Lipid not controlled (LDL >=100 mg/dl)	30	159	1.901 (0.784,4.613)	0.155	1.361(0.506, 3.658)	0.541
GCS	Mild (13–15)	10	176				
	Moderate (9–12)	14	82	1.838(0.809,4.179)	0.146	1.924(0.532, 6.964)	0.319
	Severe (<8)	26	70	3.538(1.692,7.4)	0.001	12.690(2.603, 61.873)	0.002*
NO DCMP		45	316				
DCMP		5	13	1.910 (0.756,4.828)	0.171	3.875 (0.995, 15.090)	0.051
No chronic liver disease		43	259				
Chronic liver disease		3	4	3.343 (1.022,10.936)	0.046	4.969 (1.192, 20.704)	0.028*
No HIV/AIDS		48	324				
HIV/AIDS		2	4	2.678 (0.646,11.095)	0.174	8.302 (1.585, 43.502)	0.012*
No aspirational pneumonia		12	243				

Aspirational pneumonia	38	84	4.707 (2.442,9.073)	0.000	2.602 (1.085, 6.242)	0.032*
No hypokalemia	30	301				
Hypokalemia	20	27	3.767 (2.129,13.618)	0.000	1.179 (1.112, 3.373)	0.013*
No acute renal failure	27	319				
Acute renal failure	23	9	7.772 (4.436,9.073)	0.000	6.114 (1.817, 20.576)	0.003*
No hemorrhagic transformation	39	315				
Hemorrhagic transformation	11	13	3.425 (1.745,6.723)	0.000	2.335 (0.783, 6.961)	0.128
Without atrial fibrillation	24	252				
Atrial fibrillation	26	76	2.033 (1.156,3.575)	0.014	1.104 (1.015, 5.404)	0.003*

*Key: GCS -Glasgow Coma Scale; LDL-Low-density lipoprotein; DCMP-Dilated cardiac myopathy; AF-Atrial fibrillation; AHR-Adjusted hazard ratio; CHR- Crude hazard ratio, * The Statistically significant predictor of mortality with $p < 0.05$ in multivariate cox regression analysis*

5.5 Predictors for length of hospital stay

The length of hospital stay was assessed from the day the patient was admitted to the hospital with acute ischemic stroke or, if the patient was already hospitalized for another condition, from the day of the actual stroke to the day the patient was transferred from the stroke unit to home, another hospital, or a rehabilitation facility. The median length of hospital stay was 5 days, ranging from 1 to 18 days.

A linear regression analysis was performed to assess the predictors of the length of hospital stay. Variables with p <0.2 level in the bivariate linear regression model; the presence of atrial fibrillation, aspirational pneumonia, post-stroke depression, acute gastrointestinal hemorrhage, the presence of valvular heart disease, the presence of deep venous thrombosis, and newly diagnose Diabetes mellitus, were further treated multivariate linear regression analysis to identify independent predictors of prolonged hospital stay (Table 7).

For the current model, multicollinearity problems were not present in the models because all tolerance levels were higher than 0.2 and the variance inflation factor (VIF) values for all independent variables were <10. Since the data in all of the models' standardized residuals were normally distributed, the requirements of the linear regression model were also fulfilled ($p< 0.05$).

Hence, the results of the multivariate linear regression analysis showed that the number of patients who experienced deep vein thrombosis increased by one, length of hospital stays increased by 7.337 (β=7.337, 95%CI: (1.226-13.448)). Furthermore, the length of hospital stays was increased by 2.089 times (β=2.089, 95%CI: (1.178-3.000)) for the number of patients who acquired aspiration pneumonia during hospitalization increased by one.

In addition, the number of patients with the presence of atrial fibrillation increased by one the length of stay increased by 1.696 (β=1.696, 95%CI: (0.851-2.542)). Besides, the number of patients diagnosed with post-stroke depression, increased by one the length of hospital stays increased by 4.831 (β=4.831, 95%CI: (2.330-7.332)).

Table 7 Independent predictors of length of hospital stay in patients with an acute ischemic stroke

Variables	Category	Unadjusted slope (β) of regression line		Adjusted slope (β) of regression line	
		β (95% CI)	p-value	β (95% CI)	p-value
Newly Diagnose Diabetes mellitus	No	Reference			
	Yes	1.875 (-0.516,4.266)	0.124		
Deep venous thrombosis	No	Reference			
	Yes	8.447 (1.847,15.106)	0.012	7.337 (1.226,13.448)	0.019*
Aspirational pneumonia	No	Reference			
	Yes	2.481 (1.531,3.431)	0.000	2.089 (1.178,3.000)	0.000*
Acute gastrointestinal hemorrhage	No	Reference			
	Yes	2.810 (-1.061,6.681)	0.154		
Atrial fibrillation	No	Reference			
	Yes	1.904 (1.003,2.806)	0.000	1.696 (0.851,2.542)	0.000*
Valvular heart disease	No	Reference			
	Yes	1,554 (0.548,2,559)	0.003		
Post-stroke depression	No	Reference			
	Yes	5.225 (2.533, 7.918)	0.000	4.831 (2.330,7.332)	0.000*

** The Statistically significant predictor of length of hospital stays with $p < 0.05$ in multivariate linear regression analysis using the backward method*

6 Discussion

This study assesses the clinical characteristics and outcomes of patients with AIS and AF. In this study, clinical characteristics such as GCS of less than 8, comorbidity with any type of valvular heart disease, coronary heart disease, and in-hospital stroke-related complications were higher in patients with acute ischemic stroke and atrial fibrillation.

The current study found that mortality from AIS plus AF was approximately three times higher than that of the acute ischemic stroke alone group at hospital discharge (25.5% versus 8.7%, $p<0.001$). The incidence rate of mortality for acute ischemic stroke plus AF was 38 per 1000 person-days. In contrast, the mortality rate for acute ischemic stroke without AF was 17 per 1000 person-days. There were also statistically significant differences in median survival time between patients with acute ischemic stroke plus AF and acute ischemic stroke alone (P=0.011). The Cox regression analysis revealed that Glasgow Coma Scale (GCS) less than 8, aspirational pneumonia, hypokalemia, Acute Renal Failure, HIV/AIDS, chronic liver disease and Atrial Fibrillation were independent predictors of in-hospital death. Besides, linear regression analysis reported that the presence of AF, post-stroke depression as well as stroke-related comorbidities such as aspiration pneumonia and Deep venous thrombosis (DVT), were significant predictors of a prolonged hospital stay.

This study found that 26.9 % AIS patients were diagnosed with AF. These results indicate that the frequency of AF in patients with AIS is higher in the study area than study conducted in China, Bangladesh, and Malaysia, AF was found in 20.3%,17.6%, and 6.5% of study participants respectively [15, 38, 39]. This difference may be explained in part by differences in patient background, ethnicity and due to a difference in the study area. Of 102 acute ischemic strokes with AF patients, 52.9 % were female patients while 47.1 %, were male patients. a Multicenter Multinational Hospital–A based study in Europe has also reported 57.9% females [40]. However, in contrast to our finding, Mallick et al [15] reported male predominance. Furthermore, the current study revealed that patients with AF were older at the time of stroke onset, with a mean age at stroke onset of (65.75 years ±16.4years vs 63 years ±13.58 years). The findings were consistent with those of previous studies conducted in Kenya [55], Cameroon [16], and Bangladesh [15], but

the Multicenter Multinational Hospital-Based Registry in the European community [40] revealed a somewhat higher mean age at a stroke on set (77.3 years ±9.6 years vs 70.6 years ±12.9 years). The disparity could be explained by difference in sample size, research area, and age disparities in the studied population.

6.1 Clinical characteristics

In this study, the clinical characteristics of each patient at hospital admission and throughout their hospitalization were assessed. Regarding with stroke severity at the time of hospital admission, despite, the NHISS was proven to be more accurate than the GCS to assess stroke severity [56], GCS was the only functional stroke severity assessment scale utilized by physicians in our study area. Hence the current study found that severe stroke with GCS less than 8 was significantly higher with a patient in the AF group (83.3% vs 4%, $p<0.001$). The findings were consistent with those of studies by Sen Lin et al [9], and Niamh et al [57], who revealed that severe stroke was linked with the atrial fibrillation group and they reported stroke severity with higher median NIHSS score at the time of hospital admission (10 vs 4, $p<0.001$,) and (6 vs 4, $p=0.008$) respectively.

The present study shows that 58 (56.9%) AIS patients with AF suffered from valvular atrial fibrillation (VAF) due to the presence of valvular heart disease (CRVHD, prosthetic heart valve, mechanical heart valve), while (43.1%) of patients in this group suffered from non-valvular atrial fibrillation. Which is significantly higher than the study conducted in Italy after the incidence of acute ischemic stroke. The study demonstrated VAF was reported only in 7% of acute ischemic stroke patients [41]. This difference may be explained due to the high incidence of rheumatic heart disease in most developing countries including Ethiopia.

In addition, the study showed that compared to patients without AF, patients with AF were a higher proportion, coronary heart disease, and with a lower frequency of hypertension, and hyperlipidemia (LDL >=100 mg/dl). This finding is supported by the study by Niamh et al [57] and Lin et al [9].

The current study also showed that patients with AF are more likely to have stroke-related complications like acute renal failure (22.5% vs 3.3%), hypokalemia (18.6% vs 10.1%), aspirational pneumonia (42.2% vs 28.7%), and hemorrhagic transformation (11.8% vs 4.3%). This finding was in line with the Austrian Stroke Registry [58], and Lin et al [9] showed that there were an association between the development of medical complications and acute ischemic stroke with atrial fibrillation patients.

6.2 Mortality and its predictors

The study found the overall in-hospital mortality rate of AIS were 13.22%. In-hospital mortality rate of AIS patients with AF were higher. The incidence rate of mortality for acute ischemic stroke with atrial fibrillation was 38 per 1000 person-day. The in-hospital survival rate was 30.2% with a mean survival time of 12.75 days (95% CI: 11.241 -14.268). On the other hand, the incidence rate of mortality for AIS without AF was 17 per 1000 person-day. The in-hospital survival rate was 52.8 % with a mean survival time of 15 days (95% CI: 13.523 -16.59). The case fatality of AIS with the AF group was approximately 3 times than without the AF group (25.5% vs 8.7%, $p<0.001$). These results fall in line with results of previous two studies, Ritu et al [59] and Kannikar et al [44] report high case fatality in the AF group (17% vs 8%) and (14.1 % vs 6.2%) respectively. Even though we assess in-hospital mortality rate with the median (IQR) follow-up day of 5.49 days, the mortality rate of AIS with AF in the study area is higher than that of the 28-day mortality rates study in Japanese [45] AIS patients with and without AF (11.3% vs. 3.4%; $p < 0.001$) and 30 days mortality rate in Canadian perspective registry of 12,686 AIS patients with AFs (22.3%vs10.2%; $p<0.001$) [60]. The possible reasons may be due to the AF group having high hospital stroke-related complications, as well as a higher mean age, the difference in study design, sample size, AIS care in health system and stroke severity.

In the current study, patients who had a GCS of less than 8 during hospital admission was a predictor of in hospital mortality which increased the hazard of death by 12.6 times (AHR=12.69, 95%CI: 2.603-61.873; $p<0.002$). This finding is supported by studies conducted by Mittal et al [61] , Shah et al [62] and Bhatia et al [63] reported GCS score of <8 as a predictor of the mortality.

This study identified aspirational pneumonia as another predictor of mortality. Patients who acquired aspirational pneumonia during hospital stay was 2.6 times increased chance of in-hospital mortality (AHR=2.602, 95%CI: 1.085-6.242; p=0.032). A consistent finding was reported from Thailand [44] showing Aspirational pneumonia (AOR=2.60, 95%CI: 2.38–2.84) were independent predictors of in-hospital mortality. Similar studies in the Netherlands [47] and Taiwan [48] found that a day of pneumonia following an acute ischemic stroke was a significant predictor of mortality or poor outcome at discharge.

In the current study, patients who developed Stroke-related complications of acute renal failure during their hospital stay were 6.114 times more likely to quickly dying (AHR=6.114, 95%CI: 1.817, 20.576; p=0.003) as compared with those of patients who do not develop ARF during the hospital stay. This finding is supported by studies conducted by Fahad et al [49] acute kidney failure were independent predictors of in-hospital mortality (AOR=2.2, 95% CI:2–2.2; P<0.0001). Similarly Khatri et al [50] also report acute renal failure was associated with increased in-hospital mortality in a patient with acute ischemic stroke (AOR=3.08, 95%1.49-6.35; P<0.0001). The similarity might be due to the fact that acute ischemic stroke patients are at risk of acute kidney failure due to volume depletion, contrast exposure, and pre-existing comorbid diseases. Physiologic imbalances and altered metabolism related to ARF include increased inflammation and oxidative stress, which could both hypothetically worsen outcomes [64, 65].

Studies shows that Hypokalemia is a common electrolyte abnormality and complication encountered in hospitalized patients [66]. In the present study patients who had hypokalemia during their hospital stay increased the hazard of in-hospital mortality by 17.9% (AHR=1.179, 95%CI: 1.112, 3.373; p=0.013. Consistent with the present study, the study by Gariballa and his colleagues [67] reports that lower plasma potassium (for a 1 mmol/L lower plasma potassium concentration from the normal value) on admission to the hospital was associated with an increased chance of in-hospital death, by 73% (AHR 1.73 (95% CI: 1.03 − 2.9). Similarly, Fan et al [66] also report that Hypokalemia was associated with poor outcomes (AOR=2.42, 95% Cl=1.21–4.86, P=0.013). This may be due to the physiological consequences of hypokalemia on membrane depolarization and calcium ion influx, leading to events such as vasoconstriction and neuronal damage, which could be directly related to stroke mortality [68, 69].

The current study found that patients with HIV/AIDS comorbidity increased the risk of in-hospital mortality by 8.302 times (AHR=8.302, 95%CI: 1.585, 43.502; p=0.012). This finding is consistent with research conducted in Thailand, which found that HIV/AIDS was linked with a greater risk of in-hospital mortality (AOD=4.12; 95% CI: 196-866; P=0.001) [70]. This may be because HIV infection increased the chance of getting an infection while in acute hospitalization and was associated with higher inpatient mortality.

This study also revealed that patients with chronic liver disease during hospitalization had a nearly 5-fold higher risk of in-hospital mortality (AHR=4.969, 95%CI: 1.192-20.704; p=0.028) than those without a chronic liver disease concomitant condition. Similar to our findings, study conducted in America [71] showed that liver impairment was highly linked with in-hospital mortality in acute ischemic stroke patients (AOD=1.60; 95% CI: 1.51-1.71; P0.001). This may be in part can be explain patients with chronic liver disease may predisposed to decompensation due to non-neurological conditions like alcohol withdrawal [72]. Moreover, it may be due to potential interactions between chronic liver disease and stroke therapy may directly impact or restrict the prescription of some drugs [71].

The results of this study also showed that AF was a predictor of in-hospital fatalities. However, AF was not the only significant independent predictor of death. When AF was present, hospital mortality increased by 10.4% (AHR=1.104, 95% CI: 1.015, 5.404; p=0.003) which was a substantial increase. This finding is consistent with study by Kimura et al [45] according to this study AF was associated with an increased risk of hospital mortality with an adjusted odds ratio of 1.27 (AOR=1.27, (95% CI, 1.06-1.51; P=0.0001). Similarly, Thygese and his colleagues [43] also reported that AF raised the risk of death within 30 days by 1.55 (AHR=1.55, 95% CI: 1.20-2.01; p=0.013).

6.3 Length of hospital stay and its predictors

When managing acute stroke patients in hospitals, the length of stay is the primary factor that influences costs [73]. To achieve high patient turnover and subsequently to provide more efficient

acute care for stroke patients, it is necessary to shorten the stay and make much better use of the bed and personal resources [74].

The multiple regression analysis reported that the presence of atrial fibrillation, post-stroke depression as well as stroke-related complications such as aspiration pneumonia and DVT, were significant predictors of a prolonged hospital stay.

This study showed that the number of patients who experienced DVT increased by one, length of hospital stays increased by 7.337 (β=7.337, 95%CI: (1.226-13.448)). Consistent with this finding Arboix [51] reported that DVT was the most relevant vascular complication that prolonged length of stay (AOR =2.68 (1.37, 5.26) P=0.004). The possible justification for this might include the requirements to establish an appropriable diagnosis and the duration required to reach a therapeutic INR value for an oral anticoagulant.

The current study also demonstrated that the length of hospital stays was increased by 2.089 times (β=2.089, 95%CI: (1.178-3.000)) for the number of patients who acquired aspiration pneumonia during hospitalization increased by one. It considerably extended hospital stays, as compared with those patients who did not acquire aspiration pneumonia during their hospital stay. Similar to this finding Arboix [51] reported that stroke-associated infection, particularly aspirational pneumonia, was independently associated with acute ischemic stroke and prolonged length of stay (AOR=1.78 (1.37,2.33) P<0.001).

The current study also reported that in the presence of AF, there was a 1.696-fold (β=1.696, 95%CI: (0.851-2.542)) increase in LOS. Previous studies that had also reported that patients with acute ischemic stroke and AF had a longer hospital stay [42, 43, 45]. A longer duration of stay in patients with AF may be owing to a higher risk of in-hospital medical complications, which would necessitate further treatment before the patient is discharged.

The diagnosis of post-stroke depression is extremely rare and often neglected, and its importance in relation to stroke outcomes is ignored and underestimated [75]. In the current study, it was found patients diagnosed with post-stroke depression during their hospitalization had a 4.831-fold increase in length of hospital stay (β=4.831, 95%CI: (2.330-7.332)). Consistent with this finding,

the retrospective observational study by Huanguang Jia [76] reported that patients with post-stroke depression had significantly longer inpatient stays, outpatient visits, and repeat admissions within one year of their acute stroke. Notably, poststroke depression increased the length of inpatient stay by 1.2-fold compared with patients without poststroke depression. This could be due to the fact that depressed patients may not want to leave the hospital. Patients with depression may hope for more support from medical professionals and thorough treatment in an inpatient unit [77]. Another possible reason is that people who suffered from depression after the stroke had less functional independence in daily tasks, which may prolong the duration of hospitalization [78].

7 Limitations of the study

The major limitation of this study was the short-term follow-up only kept track of in-hospital outcome. Because this was a retrospective study, it may not be possible to traced all the necessary information from the patient chart. The small sample size due to the limited number of admissions, may also affect the statistical power of the study. The effect of some potential predictors of mortality and length of stay, such as acute ischemic stroke etiology, and atrial fibrillation subtype were not fully documented in the patient's medical record, as a result they were totally left out of the analysis.

8 Conclusion

In this study, clinical characteristics such as GCS of less than 8, comorbidity with any type of valvular heart disease, coronary heart disease, and in-hospital stroke-related complications were higher in patients with acute ischemic stroke and atrial fibrillation. In-hospital mortality rate for acute ischemic stroke associated with atrial fibrillation was particularly higher than patients without atrial fibrillation and had a reduced chance of survival during hospital stay. Despite the significant mortality rate among acute ischemic stroke with atrial fibrillation patients, atrial fibrillation was not demonstrated to be a strong independent predictor of death, stroke-related complications, aspirational pneumonia, acute renal failure hypokalemia and atrial fibrillation were found to be independent predictors for in-hospital mortality. The presence of atrial fibrillation, as well as stroke-related comorbidities such as aspiration pneumonia and deep venous thrombosis, and post stroke depression were significant predictors of a prolonged hospital stay.

9 Recommendation

Based on the finding of our study we give the following recommendation.

For Minster of health and Amhara Regional Health Bureau

- ✓ In order to lower the rates of in-hospital mortality in patients with acute ischemic stroke and atrial fibrillation, besides atrial fibrillation-related acute ischemic stroke prevention, programs should concentrate on lowering the serious complications associated with acute ischemic stroke, especially aspiration pneumonia, acute kidney injury, hypokalemia DVT and post stroke depression, which is significant predictors of mortality and length of stay. Hence effective strategies should be in place to curb the impacts of these factors.

For Tibebe Ghion and Felege Hiwot Comprehensive specialized hospitals

- ✓ Healthcare facilities should enhance the structure of a multidisciplinary team that focuses on risk assessment, prevention, and early treatment of in-hospital stroke-related complications, this has the potential to reduce excess mortality in acute ischemic stroke-associated atrial fibrillation and shorten the length of hospital stay.

For health care providers/ health professionals

- ✓ It would be preferable if health professionals offered preventative measures, early detection, and treatment of stroke-related complications, which could result in better outcomes.
- ✓ It would be better if health professionals focused on the early detection and treatment of post-stroke depression, as this could shorten hospital stays.

For researchers

- ✓ Researchers should conduct such a type of study prospectively, with prolonged follow-up.
- ✓ Since this study is conducted in a few hospitals further nation-wide community-based researches needed to assure generalizability of the findings.

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11 Annex

11.1 Annex I: Data collecting tool

<table>
<tr><td colspan="6">Data collection done by: _____Date_____</td></tr>
<tr><td colspan="6">Part 1: Patient socio-demographic information</td></tr>
<tr><td>MRN/card number:
_____</td><td>Date of admission

_____</td><td>Age: _____ (yrs.)</td><td>Sex:

☐Male
☐Female</td><td>Kebele: _____

Woreda: _____

Region: _____</td><td>Residence

☐Urban
☐Rural</td></tr>
<tr><td colspan="4">Marital status

☐Single
☐Married
☐Divorced
☐Widow</td><td colspan="2" rowspan="2">Religion

☐Orthodox
☐Protestant
☐Muslim
☐Catholic Others_____</td></tr>
<tr><td colspan="4"></td></tr>
</table>

<table>
<tr><td colspan="2">Employment level

☐Employed: Civil servant
☐Farmer
☐Unemployed: student.
☐Unemployed: self/own work Others specify _____</td><td>Education status

☐No formal education
☐Primary school (1-8)
☐Secondary school (9-12)
☐College/university or above</td></tr>
<tr><td colspan="3">Part 2: Baseline characteristics of acute ischemic stroke patients with atrial fibrillation and those without atrial fibrillation</td></tr>
<tr><td rowspan="2">Hypertension
☐Newly diagnosed
☐Known hypertensive patient

Pulmonary disease
☐Chronic obstructive pulmonary disease
☐Asthma

Cystic fibrosis</td><td>Diabetes mellitus: _____
☐Newly diagnose
☐Known DM patient</td><td rowspan="2">Alcohol intake / abuse
☐Never
☐Former drinker before one year
☐Current alcohol use

Pre-stroke medication
☐Antiplatelet
☐Antihypertensive
☐Lipid-lowering therapy
☐Antithrombotic
☐Oral anticoagulants
INR on admission
☐<2 ☐ 2-3.5</td></tr>
<tr><td>Hyperlipidemia
☐Lipid controlled (LDL<100mg/dl)
☐Lipid not controlled (LDL ≥100 mg/dl)
☐Absent

Smoking / Tobacco use
☐Current smoker
☐Former smoker before one year
☐Never smoked</td></tr>
<tr><td rowspan="2">ECG finding
☐No AF</td><td>☐Hypertensive heart disease (HHD)</td><td rowspan="2">Etiology of AIS on CT
☐Cardioembolic (CE),</td></tr>
<tr><td>☐Coronary disease (CHD, IHD)</td></tr>
</table>

☐AF or flutter ☐VAF ☐NVAF ☐Heart failure Valvular heart disease (RHD, prosthetic heart valve, Mechanical heart valve)	☐Other cardiovascular diseases such as DCM ☐Chronic liver disease ☐HIV /AIDS ☐VTE/hypercoagulable sates ☐Other comorbidities_____	☐Large artery atherosclerosis (LAA), ☐Small vessel occlusion (SVO), ☐Other determined etiology (ODE), ☐Undetermined etiology (UDE)

Part 3: Clinical status (Glasgow Coma Scale and Modified Rankin Score) during admission &time on hospital admission

Glasgow Coma Scale	**Neurologic Deficits during**
☐Mild (13–15) Mild brain injury (alert) ☐Moderate (9–12) Moderate brain injury (drowsy) ☐Severe (<8) Severe brain injury (unconscious) **Time from symptom onset to hospital admission** ☐=< 3 Hours ☐>3 hours	☐Loss of consciousness ☐Hemiparesis/hemiplegia ☐Aphasia ☐Facial palsy ☐Weakness and sensory loss ☐Urinary incontinence ☐Headache ☐Convulsions Other _____

Part 4: In-hospital treatment given

☐Thrombolysis	Other specify_____
☐Neuroprotection agents	
☐Antiplatelets	
☐Anticoagulants	
☐Antihypertensives	
☐Statins	
☐Antidiabetic drugs	

Part 5: Stroke-related complications during hospitalization of patients

☐Pulmonary infection	☐Hemorrhagic transformation
☐Urinary tract infection	☐Pulmonary embolism
☐Urinary incontinence	☐Acute gastrointestinal tract hemorrhage
☐Acute renal failure	☐Bedsore
☐Electrolyte disturbance	Other _____

Part 6: Clinical status (Modified Rankin Score) during discharge

Date for outcome happened _____/_____/_____/ (dd/mm/yy
☐Improved
☐Discharge with complications
☐Left ageist medical advice
☐Death

Attributable cause of death

☐Stroke itself

☐Complications to the Stroke

☐Hospital-Acquired Pneumonia

☐Hemorrhagic transformation

☐Recurrence Systemic embolism

☐Acute myocardial infarction

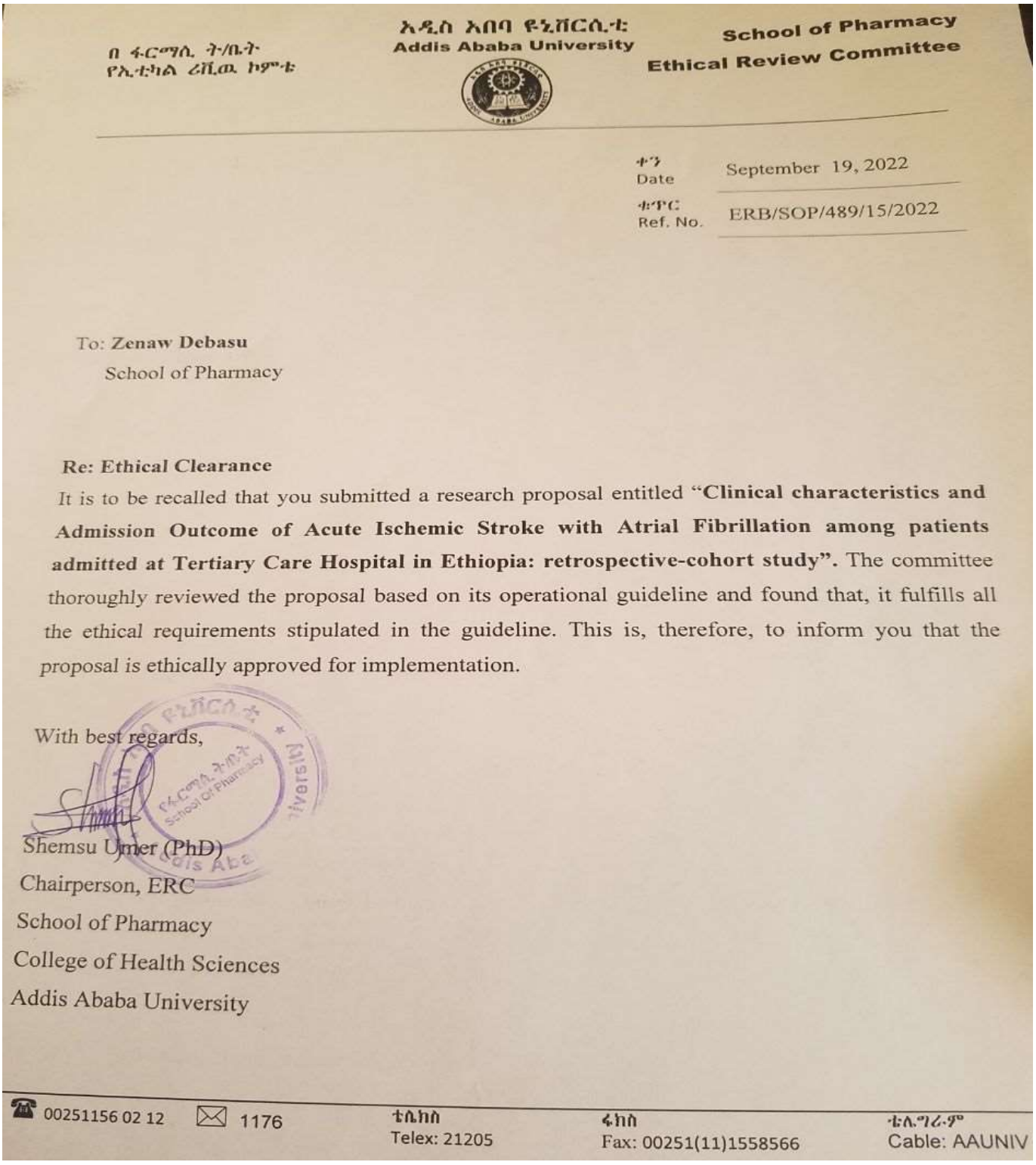
☐Chronic ischemic heart disease

☐Renal and hepatic diseases

☐Respiratory failure secondary aspiration pneumonia

Other causes_____

11.2 Annex II: Ethical clearance letter



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Addis Ababa University

School of Pharmacy
Ethical Review Committee

ቀን Date: September 19, 2022

ቁጥር Ref. No.: ERB/SOP/489/15/2022

To: **Zenaw Debasu**
School of Pharmacy

Re: Ethical Clearance

It is to be recalled that you submitted a research proposal entitled "**Clinical characteristics and Admission Outcome of Acute Ischemic Stroke with Atrial Fibrillation among patients admitted at Tertiary Care Hospital in Ethiopia: retrospective-cohort study".** The committee thoroughly reviewed the proposal based on its operational guideline and found that, it fulfills all the ethical requirements stipulated in the guideline. This is, therefore, to inform you that the proposal is ethically approved for implementation.

With best regards,

Shemsu Umer (PhD)
Chairperson, ERC
School of Pharmacy
College of Health Sciences
Addis Ababa University

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