



Assessment of the magnitude of non-valvular atrial fibrillation and associated factors among hypertensive patients at Saint Paul's Hospital Millenium Medical College Cardiac Referral clinic, Addis Ababa, Ethiopia.

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Assessment Of Magnitude Of Non-Valvular Atrial Fibrillation And Associated Factors
Among Hypertensive Patients At The Cardiac Referral Clinic Of Saint Paul's Hospital
Millenium Medical College, Addis Ababa, Ethiopia.

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List Of Acronym And Averbiation

ACEI→Angiotensin converting enzyme inhibitor
AF→ Atrial fibrillation
AHA/ACC→American Heart Association/American College of Cardiology
ARB→angiotensin II receptor blocker
CCB→ Calcium Chanell blocker
CHD→ Coronary heart disease
CHF→ Congestive heart failure
CKD→ Chronic kidney disease
COPD→Chronic obstructive pulmonary disease
CRC→Cardiac referral clinic
DBP→Diastolic blood pressure
DC→ Data collector
DM→Diabetes Mellitus
DOAC→ Direct oral anticoagulant
DS→ Data supervisor
ECG→ Electrocardiogram
ECHO→ Echocardiograph
EF→ Ejection fraction
GDB→Global disease burden
HFrEF→ Heart failure with reduced ejection fraction
HHD→Hypertensive heart disease
HTN→ Hypertension
IHD→ Ischemic heart disease
IVSD→Interventricular septal diameter
LAD→ Left Atrial Diameter
RHD→Rheumatic heart disease
SBP→ Systolic Blood Pressure
SPHMMC →Saint Paul’s Hospital Millenium Medical college
TFT→Thyroid function Test
UA→Uric Acid
VHD→ Valvular heart disease

Abstract

Background: Atrial fibrillation is the most common clinically relevant arrhythmia treated globally which is characterized by disorganized and ineffective atrial contraction. It is associated thromboembolic complications and HF which leads to increase risk of mortality and morbidity. Atrial fibrillation accounts for 20-30% of ischemic stroke and 10% of cryptogenic stroke and increase mortality by 1.5 to 1.9 times from the general population. Hypertension is one independent risk factor associated with atrial fibrillation.

Objectives: The main objective of this study was to assess the magnitude of non-valvular atrial fibrillation and associated factors among hypertensive patients.

Method: An institution based cross-sectional study was conducted on 201 hypertensive patients at Saint Paul's Hospital Millennium Medical college cardiac referral clinic. Study participants were selected by a systematic random sampling method. Interviewer administered structured questionnaire was used for data collection. Data entry and analysis was done by EPI DATA version 7 and SPSS version 26.0 respectively. Means, standard deviations, and percentages was computed for descriptive analysis and multivariate logistic regression analysis performed to determine factors associated with atrial fibrillation. Variable relationships are significant at a P value <0.05.

Result: This study was done on 201 hypertensive patients with age range of 26-91 years and mean age of 56.38 years, among which 118 (58.9%) were females. The prevalence of non-valvular atrial fibrillation was 12.9%. Age ≥ 50 years (AOR=8.6, 95%CI 2.74, 26.91), LVH (moderate and severe) (AOR=4.74, 95% CI: 1.32, 16.94), having diabetes mellitus (AOR: 8.23, 95% CI (2.75, 24.61) and having dyslipidemia (AOR=3.84, 95% CI: 1.40, 10.53) were significantly associated with non-valvular atrial fibrillation.

Conclusion and recommendation:

Non-valvular atrial fibrillation is common and found in more than one-tenth hypertensive population. Age ≥ 50 years, hypertensive heart disease, DM and dyslipidemia are particularly at high risk of non-valvular atrial fibrillation which need a clinician's special attention for early diagnosis and management.

Key word: atrial fibrillation, hypertension, Electrocardiogram

CHAPTER ONE

1. Introduction

1.1 Background of the study

Atrial fibrillation (AF) is the most frequently treated arrhythmia worldwide. It is supraventricular arrhythmia characterized by irregular uncoordinated atrial electrical activation and consequently ineffective atrial contraction. AF affects nearly 43.6 million of the global population from 2016 estimate(GDB). Prevalence is between 2 and 4% of adult population and life time risk of an individual to develop AF is 1 in 3[1] but different in different population, higher in western society but lower in Asia and Africa. In US its prevalence is 1% [2] and Sweden 2.9% in adult age > 20 years[3] and in China is 0.65% in both sex, with slight male predominance[4].

Because people live longer and having multiple comorbidity, AF becomes major global healthcare problem that is increasing in prevalence and incidence worldwide[5]. This was seen from increasing in the prevalence of AF within six years by more than 10 million from 33.5 million which was seen 2010 GDB[5] data to 43.6 million from 2016 GDB estimate[6].

Atrial fibrillation is a significant health concern since it is linked to a cardioembolic stroke, which accounts for 20–30% of ischemic strokes and 10% of cryptogenic strokes, clinically significant tachyarrhythmia, which can lead to hemodynamic instability and death, tachycardia-induced cardiomyopathy, cognitive decline, depression, and a poor quality of life[1].

The exact etiology of AF is unknown, but different risk factors have been identified so far. These include aging, hypertension (HTN), diabetes mellitus(DM), congestive heart failure(CHF), congenital heart disease(CHD), and valvular heart disease[7]. Other independent risk factors include male sex, left ventricular hypertrophy(LVH), obesity and excessive alcohol consumption[8]. Age is a strong risk factor for AF and it affects over 10% of the US population over the age of 80[9]. Chronic kidney disease (CKD) with or without albuminuria is also found to be independently associated with increased risk of AF[10]. Rheumatic heart disease is prevalent in certain resource-limited areas and is strongly associated with AF[11].

AF is usually asymptomatic and the spectrum of symptoms is broad most common presentations are palpitations, fatigue, and dyspnea. Other less common symptoms include weakness, dizziness, lightheadedness, presyncope or syncope and angina. Some patients present may present with stroke or another systemic embolic event as the first presentation[12]. The risk of

stroke more common in asymptomatic than symptomatic AF and there is significant effort to detect asymptomatic AF in high risk individuals[13].

Atrial fibrillation is diagnosed by history, physical, and laboratory investigation to identify the underlying cause and precipitant. Electrocardiogram (ECG) documentation is required to establish the diagnosis of AF. A standard 12-lead ECG recording or a single-lead ECG tracing of more than 30 second showing heart rhythm with no discernible repeating P waves and irregular RR intervals (when atrioventricular conduction is not impaired) is diagnostic of clinical AF[1].

Atrial fibrillation is classified as paroxysmal, persistent, permanent depending the duration of AF and the patient and physician agreement no longer to attempt rate or rhythm control strategy respectively[1].

Depending on thrombotic risk and choice of anticoagulant atrial fibrillation also classified as valvular and non-valvular but there is significant ambiguity and debate between this two. Different international guideline including European society of cardiology (ESC) and American Heart Association/American college of cardiology(AHA/ACC) use “moderate-severe mitral stenosis of rheumatic origin and mechanical prosthetic valve replacement” as the only contraindications to eligibility for direct acting oral anticoagulant (DOAC) therapy which taken as valvular atrial fibrillation[14].

Atrial fibrillation has multiple risk factors as mentioned earlier but hypertension being the most common cardiovascular disease affecting nearly half of the global population increases the incidence of atrial fibrillation by 50%[15]. Around 10% hypertensive patient has atrial fibrillation [16]. There is scarcity data in Sub-Saharan Africa including Ethiopian on magnitude of AF and non-valvular AF in particular.

1.2 Statement of the problem

The available evidence shows that AF is the commonest sustained arrhythmia globally as well as in our set up and associated with significant mortality, morbidity and healthcare cost with different identified risk factors.

The global prevalence of atrial fibrillation from 2016 global disease burden estimate is around 46.3 million [3]. The prevalence may be even higher as most of patients are asymptomatic and remain undiagnosed.

There is no adequate data on the prevalence of atrial fibrillation in the developing part of world mainly Sub-Saharan Africa and it is estimated to be lower than western but associated with significant mortality and morbidity due to poor health care system.

AF has many risk factors even though the exact etiology is not known. Hypertension (HTN) is one of the most prevalent and modifiable risk factor for cardiovascular morbidity and mortality associated with different atherosclerotic disease, CKD, stroke and heart failure [6]. HTN affects nearly half of global population as of now and continue to surge make it major public health threat and importance [17]. AF is strongly associated with HTN and both are increasing in prevalence and incidence. HTN and AF has complex and multidirectional relation including structural, hemodynamic, neuroendocrine, and autonomic mechanisms. Hypertension provokes excessive fibroblasts proliferation and increased collagen accumulation, stimulates cardiomyocytes apoptosis and inflammation, leading to diffused fibrosis and left ventricular hypertrophy development [17].

In study done in Tanzania, the prevalence AF in HTN patient was 10.2% [16] and in other cross-sectional community-based study which was done in Ethiopia, Jimma Town among those of age > 40 years, the prevalence of AF was relatively low 4.3% which increase with age and HTN was one of the strong risk factor associated with AF [18].

Atrial fibrillation confers a substantial mortality and morbidity from stroke, thromboembolism, heart failure, and impaired quality of life[4]. With the increasingly elderly population in the developed world, as well as improvements in the management of myocardial infarction and heart failure, the prevalence of atrial fibrillation is increasing, which resulting in a major public-health problem [5].

1.3 Significance of study

AF associated with significant health problem and if identified and treated early most of the complication can be avoided. Therefore, it is wise to invest on and produce adequate evidence-to provide better care for these population and avoid its complication.

Even though it is the hot issue upon which multiple researches were done and being done globally, there are only few data are available in our part of the world including Ethiopia. There are few data on AF in general in Ethiopia but no published data available for non-valvular AF to my knowledge. To fill this gap and to be the base for upcoming research in this area magnitude of non-valvular AF among hypertensive patient is chosen for this post graduate thesis.

CHAPTER TWO

1. Literature review

2.1 Magnitude of AF

Evidences show that AF is estimated to increase in the coming decades. AF is important public health problem both in developed and developing countries as it associated significant morbidity and mortality. Thromboembolic event mainly ischemic stroke is the most important complication of AF followed by HF and tachycardia induced cardiomyopathy[1].

Global Burden of Disease data on the prevalence of AF worldwide was done from a comprehensive analysis of population-based research from 1980 to 2010. During that time the burden of AF, expressed as disability-adjusted life years, rose by 18.8% for men and 18.9% for women and the mortality rate related to AF increased 1.9 times (95% UI, 1.8-2.0) for women and 2 times (95% UI, 2.0-2.2) for males [5].

From 2019 global disease burden estimate AF/AFL shows significant increase with 4.72 million new cases, 0.315 million deaths, and 8.39 million DALYS, and there were 59.70 million AF/AFL patients globally. High systolic blood pressure, a high body mass index, drinking, smoking, and a diet high in sodium were the risk factors with the greatest impact on fatalities and DALYs attributed to AF/AFL. It is also projected to increase in the coming decade and between 2030 and 2034 there will be 16.08 million and 16.85 million male and female cases of AF/AFL, 1.01 million and 1.49 million male and female deaths respectively [11]. This certainly demonstrates how AF is increasing alarmingly and keep on being major public health threat.

2.2 Impact of AF

AF increases mortality which was demonstrated from Framingham heart study cohort where the AOR for death of 1.5 (95% CI, 1.2 to 1.8) in men and 1.9 (95% CI, 1.5 to 2.2) in women after adjusting to other confounders. Despite the prevalence of AF common in men than women as which was shown in different studies, the mortality is more common in women[17].

There was one systematic review done to evaluate the prevalence of AF and related stroke risk factors in Africa and to gauge the necessity for screening. The prevalence of AF seems to be lower and at younger age than those reported in developed part of the world. The number found

in this review is highly likely underestimation due to the several limitations of studies included[18].

In other retrospective hospital based study done in Senegal, the overall prevalence of AF was 5.4% and which accounted for 66% of heart rhythm disorders[19]. In other hospital based study in Kenya the prevalence the prevalence of AF among medical patient was lower 0.7%: among which 15% presented with thromboembolic event[19].

Other community based cross-sectional study was done semi-urban area in southern Ethiopia on 3000 patient with median age of 31 and men account 65%, the prevalence of AF was 0.4% and in those above the age of 40 years it was 1% and above 70 years it was 6.6%[20].

Prospective cohort was conducted to see mortality, stroke and cost of AF patient with other CVD compared with age-sex matched group of patients without AF over three years period. This cohort shows the overall mortality were higher in patients with AF. There were 28% increase in mortality in male of age 65-74 years. The risk of stroke was higher in patient with CVD but there was no significant difference in male with AF and without AF. But in female the risk of stroke was higher in those with AF than without AF. The health care cost were also significantly higher those patient with AF compared without AF [21].

A systematic review and meta-analysis of 12 studies of 99,999 including RCT, cohort studies and case series was done to see the impact AF type (paroxysmal vs non paroxysmal) on thromboembolic risk, mortality and bleeding. The unadjusted risk ratio (RR) for thromboembolism in non paroxysmal AF vs. paroxysmal AF was 1.355. In the study subset off oral anticoagulation, unadjusted RR was 1.689. The overall multivariable adjusted hazard ratio (HR) for thromboembolism was 1.384. The overall unadjusted RR for all-cause mortality was 1.462. Multi- variable adjusted HR for all-cause mortality was 1.217. Rates of bleeding were similar, with unadjusted RR 1.00 and adjusted HR 1.025[22].

2.3 Associated factors of AF

There different risk factors which increase the incidence and prevalence AF, among Which HTN with its complication is one of most strong risk factors which was seen in different observational studies and systematic reviews.

In the Framingham cohort study, which examined the development of chronic atrial fibrillation in relation to antecedent cardiovascular disease and other risk factors with twice per annum follow up for 22 years. Hypertensive cardiovascular disease was the most frequent antecedent disease which accounts 58.4% of patient who develop AF [17].

A large prospective AF prospective registry which was done in the emergency department of 46 nations and 146 site hypertension was the most common risk factor reported which was found 62.0% of AF patients. From this registry there is difference hypertension prevalence where those from Eastern Europe had the highest hypertension prevalence 80.7%, while those in Western Europe, India, China, Southeast Asia, the Middle East, and Africa had lower prevalence, with India having the lowest prevalence 41.6%[21]. Other risk factor identified from that registry were HFrEF or LVSD(36.2-60.5), VHD (10.7-46.7%), RHD (1-15%), DM (15.5-36.5%), OSA (3.9%), obesity (7.2% and hyperthyroidism (3.7%)[21].

A study which was done in Tanzania in 2020 to see the burden of atrial fibrillation among hypertensive patient shows the prevalence of AF was 10.25% and both dilated left atrial size and lower ejection fraction (<50) were identified as independent predictors of AF[16].

A community based cross-sectional study in Sodo, Ethiopia done among 3000 patient the prevalence of AF was 0.43 and HTN was identified as significant risk factor which was found in 23% AF patient and 31% of in patient who has indication for anticoagulation by CHA₂DS₂ VASC [20].

Another cross-sectional study done Gondar University on prevalence and predictor of stroke among atrial fibrillation patient, hypertension was present in one fourth of the patients[22].

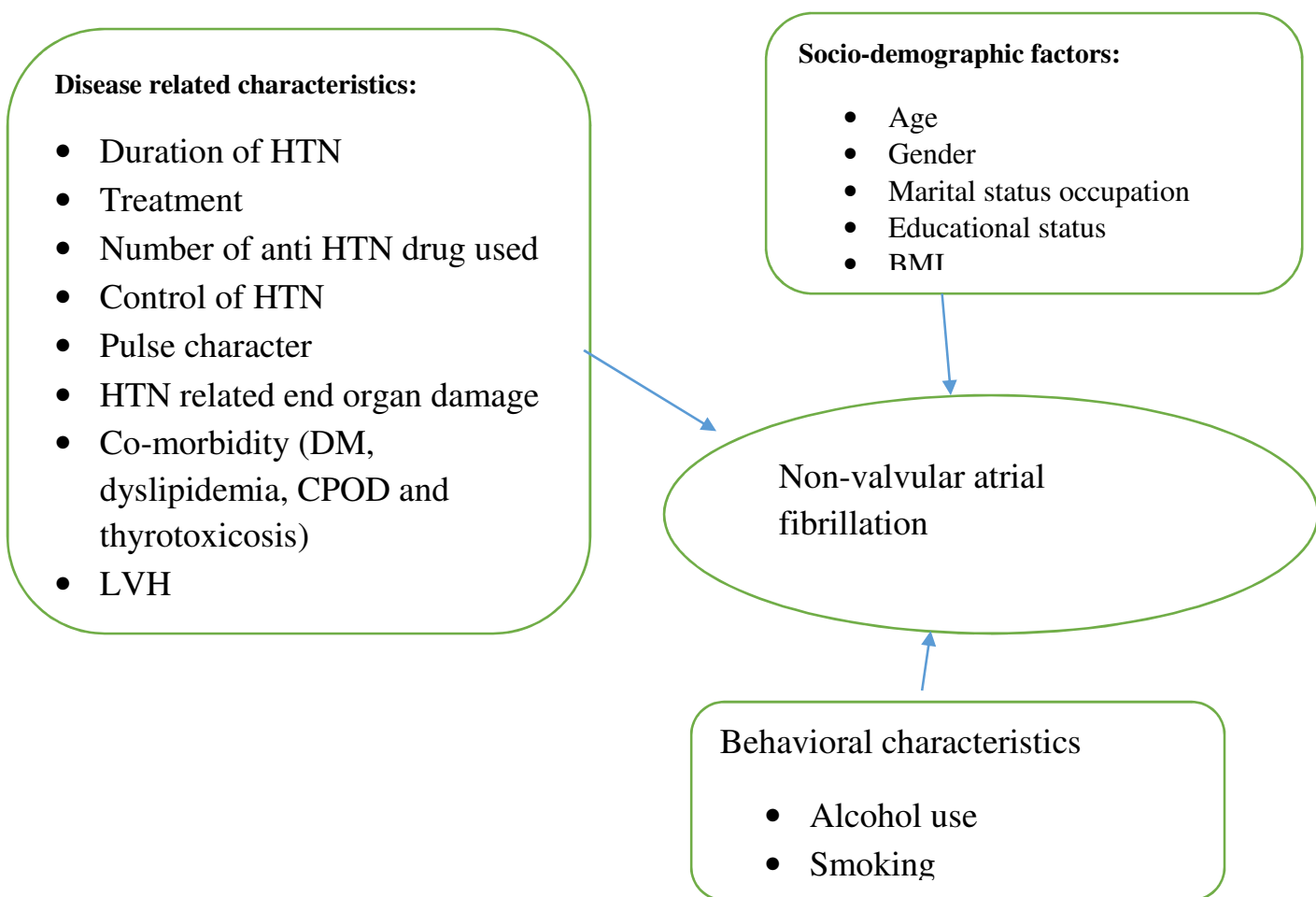
Even though the association between HTN and AF was established the exact pathogenesis is not well understood. There were systematic review of 11 animal studies which were done to establish the pathogenesis of AF in HTN shows that persistent elevation afterload which leads to LVH and increase back atrial pressure atrial cardiomyopathy with subtle electrophysiologic change which serve as a substrate for PAC and atrial fibrillation[23].

Another animal study to which was done on rat to see the effect of HTN on AF with hypothesis of HTN alter atrial myocyte electrical conduction and Ca²⁺ handling shows HTN induces early subcellular myocyte Ca²⁺ changes which initially don't cause conduction abnormality but later result in arrhythmogenic Ca²⁺ alternans which show the link between HTN and AF[24]

2.4 Conceptual frame work

Non-valvular atrial fibrillation is the commonest sustained rhythm disorder which has several risk factors mentioned in different literature. Sociodemographic factors, duration and control HTN, HTN associated end organ damage and comorbidities like, DM, dyslipidemia, obesity, and COPD can affect the prevalence of NVAf. The conceptual frame work depicted in the figure below (Figure 1)

FIGURE 1: CONCEPTUAL FRAME WORK NVAf IN HTN PATIENT[25][26], [27]



CHAPTER THREE

2. Objectives

3.1 General objective

To assess the magnitude of non-valvular atrial fibrillation and associated factors among hypertensive patient who has active follow up at SPHMMC cardiac referral clinic, Addis Ababa, Ethiopia from August 1, 2023 to November 3, 2023.

3.2 Specific objective

1. To assess the prevalence of non-valvular AF in hypertension patient
2. To identify associated factors with non-valvular AF in hypertensive patients

CHAPTER FOUR

4. Methodology

4.1 Study design

Institutional -based cross-sectional study design was used

4.2 Study area

The study was conducted in the one of the largest hospitals of the country, named SPHMMC, which was established 75 years back during the reign of Emperor Haile Silase I by the help of German Evangelical Church to serve for the under privileged section of society and until recently it was serving for free. It is located in the heart of Addis Ababa, the capital city of Ethiopia. It is a referral hospital serving more than 5 million people. Since 2007 GC it is also serve as the main teaching hospital for both undergraduate and postgraduate program of in most medical disciplines. It is also one of the few institution where specialized clinical services that are not available in other public or private institutions are given like interventional cardiac procedures and it is the only center where renal transplant is being done in the nation so far.

4.3 Study period

The study was conducted from August 1, 2023 to November 30, 2023

4.4 Population

4.4.1 Source population

All HTN patients who are on active follow-up in adult cardiac clinic of SPHMMC from August 01, 2023 August 30, 2023

4.4.2 Study population

Selected hypertensive patients who are having regular follow up at cardiac clinic of SPHMMC from August 1, 2023 to November 30, 2023 who fulfill the inclusion criteria

4.4.3 Inclusion criteria

- Patients with HTN and regular follow up
- Age >18 years

4.4.3.2 Exclusion criteria

- Those patients with CRVHD with moderate to severe mitral stenosis
- Patient on mechanical heart valve

4.5 Sample size determination and sampling technique

All hypertensive patients having active follow-up from August 1, 2023 August 30, 2023 were recruited. There were around 600 hypertensive patients having active follow up at SPHMMC CRC per month on average. All patients that fulfill the inclusion criteria was included and a sampling frame was prepared using MRN of all patients who has HTN as one of their diagnoses, and a systematic random sampling method was used and every third of hypertensive patient selected to the sample population.

The sample size was calculated using the estimation proportion formula.

$$n = P(1-P)Z^2/E^2$$

Key

N=population size, which is HTN patients who have follow up at SPHMMC CRC in the study period

n=sample size

p=estimated proportion take 10.25% from previous studies and sample size

Z=level of confidence, which is 95% (1.96)

E=margin of error; which is 5% (0.05)

n=182+10% non-response rate and final sample size used was 201.

4.6 Study variables

4.6.1 Dependent variables

 Atrial fibrillation

4.6.2. Independent variables

- Age
- Sex
- BMI

- Alcohol
- HTN
- Duration of HTN
- Control of HTN
- LVH
- CKD
- DM
- Obesity
- Dyslipidemia
- Hyperthyroidism
- Smoking
- Uric acid
- Proteinuria

4.7 Data collection procedure

4.7.1 Data collection tool

Structured interviewer administered questionnaires which was adapted and modified from previous study done from Tanzania were used. The questionnaires were pre-tested with 5% of the total sample size to check its variability and was assessed for its clarity, length and completeness.

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4.7.2 Data collectors

Internal medicine residents above second year of training were involved in data collection. Prior to data collection, the residents were trained on how to fill the questionnaire and were followed closely for completeness and validity of the data by the investigator.

4.7.3 Data collection technique

The data was collected inside the hospital at cardiac referral clinic during the study period. The patient was identified from the hospital's EMR (electronic medical record) and HMIS (health management information system) documentation using their medical record number (MRN) as a guide to identify patients who have HTN as one of their diagnoses appointed for follow up in the month of August. After all hypertension patient who appointed for follow up was listed using their MRN the sample was taken by using systematic random sampling and those included in the

sample was asked about their permission to be included in the study and focused history was taken and physical examination was done and after that investigations were sent according the questionnaire which include RFT, TFT, urine analysis, lipid panel, uric acid if it was not done within 3 months and ECG was done at least once for those who was not previously diagnosed to have atrial fibrillation and echocardiography was sent for those who didn't have within three months of study period. After that data was fed to a structured questionnaire. Incompletely filled questionnaires due to delay in investigation result was completed by primary investigator using their MRN from EMR.

4.7.4 Data quality control

The questionnaire was pre-tested using 5% of the total sample size at SPHMMC CRC one month prior to the study period to avoid any confusion during actual data collection period. Training was given for data collectors. During data collection, principal investigator checked data for its completeness and missing information at each point. Furthermore, data was checked during entry into the SPSS before analysis.

4.8 Data processing and analysis

After the completeness of all the information on the questioners was checked, cleaned, coded, and entered using EPI DATA version 7, then analyzed with the Statistical Package of Social Sciences (SPSS) for Windows version 25. Frequencies, percentages, and mean scores were computed to summarize variables through descriptive statistics. Variables with p-value of less than 0.25 in bivariable binary logistic regressions were candidate for multivariable binary logistic regression analysis to identify significant factors for outcome variable. Variables with p-value of less than 0.05 were used to declare statistical significance and strength of association was determined by adjusted odd ratio (AOR) with 95% confidence interval (CI). The model fitness was checked using Homer-Lemeshow goodness of fit test and it was fitted ($P=0.74$). Finally, the findings presented using tables, graphs, and text.

4.9 Operational definition

Atrial fibrillation → irregularly irregular rhythm without distinct p-wave on ECG[1]

Hypertension→ at least two office BP >140/90 or having hypertension as one of their diagnosis and some form of treatment [30]

CKD→as KDIGO definition of CKD[31]

Dyslipidemia→a lipid profile with one of the following (Total cholesterol>200, TG>150, LDL>100, HDL<50 for male and <40 for female) or have dyslipidemia as one of their diagnosis and patient on medical or no-medical management[32–34].

Obesity→ defined as BMI>30KG/M²[35]

Non-valvular atrial fibrillation→ atrial fibrillation in non-moderate to severe MS and non-mechanical valve replacement[36]

LVH→ Taken as significant if it is moderate and severe from echocardiography as documented by cardiologist

Active follow up→a patient who attend his/her regular follow up

Smoking → current or previous active or passive smoking exposure of any amount[37].

Significant alcohol consumption→ more than 2 standard drink per day/14 per week for men and 1 drink per day/7 drink per week for women or history of binge drinking[38].

Controlled Hypertension→blood pressure <140/90([39], [40]) and <130/80for those with DM and CKD([31, 41])

Hypertension related end organ damage→presumed or confirmed HTN related organ damage including HHD, IHD, CKD

4.10 Ethical consideration

Ethical clearance was obtained from Institutional Review Board of SPHMMC after presenting the objective of study and its confidentiality. After obtaining the permission the data collection was commenced. All information that is obtained from the individual will be treated confidentially and will be used only for the study purpose.

4.11 Dissemination of results

The results of this study will first be presented to the staffs of Internal medicine and public health departments during the research defense presentation. It will also be submitted to the hospital's cardiology unit. Further efforts will be made to publish the information in peer-reviewed journals and make presentations in scientific conferences

CHAPTER FIVE

5. Result

5.1 Socio-demographic and behavioral characteristics of study participants

In this study, a total of 201 patient were included with the response rate of 100%. The age of participants was ranged from 26-91 years; with mean age of 56.38 years and 118 (58.9%) were females. The majority of participants 150(74.6%) are married. More than half 109(54.2% and 106(52.7%) had no formal education and overweight (BMI>25) respectively (**Table 2**).

TABLE 1: SOCIODEMOGRAPHIC, AND BEHAVIORAL CHARACTERISTICS OF PARTICIPANTS AMONG HTN PATIENT AT SPHMMC, 2023

Variable		Frequency	Percent
Age	20-50	64	31.8%
	51-70	99	49.3%
	>70	38	18.9%
Gender	Female	118	58.7%
	Male	83	41.3%
Occupation	civil servant	23	11.4%
	house wife	87	43.3%
	Merchant	19	9.5%
	Retired	35	17.4%
	self employed	22	10.9%
	Others*	15	7.5%
Marital status	Divorced	10	5.0%
	Married	150	74.6%
	Single	5	2.5%
	Widowed	36	17.9%
Educational status	No formal education	109	54.2%
	Grade 1-8	19	9.5%
	Grade 9-12	35	17.4%
	Diploma	17	8.5%
	Degree and above	21	10.4%

BMI	<18.5	7	3.5%
	18.5-24.9	73	36.3%
	25-29.9	106	52.7%
	=>30	15	7.5%
Cigarette	No	190	94.5%
smoking	Yes	11	5.5%
Significant	No	192	95.5%
alcohol use	Yes	9	4.5%

*Daily laborer, driver, Farmer, Janitor, soldier, and unemployed, BMI: Body Mass Index

5.2 Disease related characteristics of the study participants

In this study nearly one-third 68 (33.8) of the participants had less than five years duration since diagnosed with hypertension and almost all participants, 197(98%) were on pharmacological treatment and nearly two-third, 128 (63.7%) have controlled hypertension. Nearly two-third, 127(63.2%) of the participants had HTN related end organ damage and majority 114(83.2%) of them had HHD. Ninety-one (45.5%) of participant had Co-morbid disease, of which dyslipidemia and DM were the most common comorbidity which account for 60.2% and 30.5% respectively (Table 3).

TABLE 2: DISEASE RELATED CHARACTERISTICS OF STUDY PARTICIPANT AMONG HTN PATIENT AT SPHMMC, 2023

Variable		Frequency	Percent
Duration of HTN	<5 years	68	33.8
	>10 years	74	36.8
	5-10 years	59	29.4
Treatment	Non-		
	pharmacologic	4	2.0
	Pharmacologic	197	98.0
Number of anti HTN drug used	Single drug	83	41.3
	Two drugs	94	46.8
	Triple drugs	16	8.0
	Four drugs	4	2.0

Control of HTN	No	73	36.3
	Yes	128	63.7
Pulse character	Irregular	26	12.9
	Regular	175	87.1
HTN related end organ damage	Yes	127	63.2
	No	74	36.8
Type HTN related end organ damage	HHD	114	83.2
	IHD	16	11.7
	CKD	7	5.1
Co-morbidity	Yes	91	45.3
	No	110	54.7
Type of co morbidity	DM	33	30.5
	Thyrotoxicosis	3	2.8
	COPD	7	6.5
	Dyslipidemia	65	60.2

*HTN: Hypertension, HHD: Hypertensive heart disease, IHD: ischemic heart disease, CKD: Chronic Kidney Diseases, DM: diabetes mellitus, COPD: Chronic Obstructed Pulmonary Diseases

5.3 Investigation findings related to characteristics of participants

In this study, more than half of the participants 117(58.2%) had eGFR >90 ml/min/1.73 m², only six (3%) had proteinuria and 19 (9.5) Uric acid >6mg/dl. Most of the participants 191(95%) had their EF =>50% (Table 4):

Table 3: lab related characteristics among HTN patient at SPHMMC,2023

Variable		Frequency	Percent
eGFR (ml/min/1.73 m2)	NO report	17	8.5
	>90	117	58.2
	60-89	50	24.9
	30-59	14	7.0
	15-29	2	1.0
	<15	1	.5
Proteinuria	Not done	7	3.5
	No	188	93.5
	Yes	6	3.0
Uric acid (mg/dl)	Not done	35	17.4
	=<6	147	73.1
	>6	19	9.5
Echocardiogram (EF)	=> 50	191	95.0
	40-50	5	2.5
	<40	5	2.5
LVH	Yes	82	40.8
	No	119	59.2

eGFR-- estimated glomerular filtration rate, LVH—Left ventricular hypertrophy, EF—ejection fraction

5.4 Magnitude of NVAf and its characteristics:

IN THIS STUDY, THE MAGNITUDE OF NON-VALVULAR ATRIAL FIBRILLATION (NVAf) WAS 12.9% WITH 95% CI, AND 8.5-17.9) (FIGURE 2).

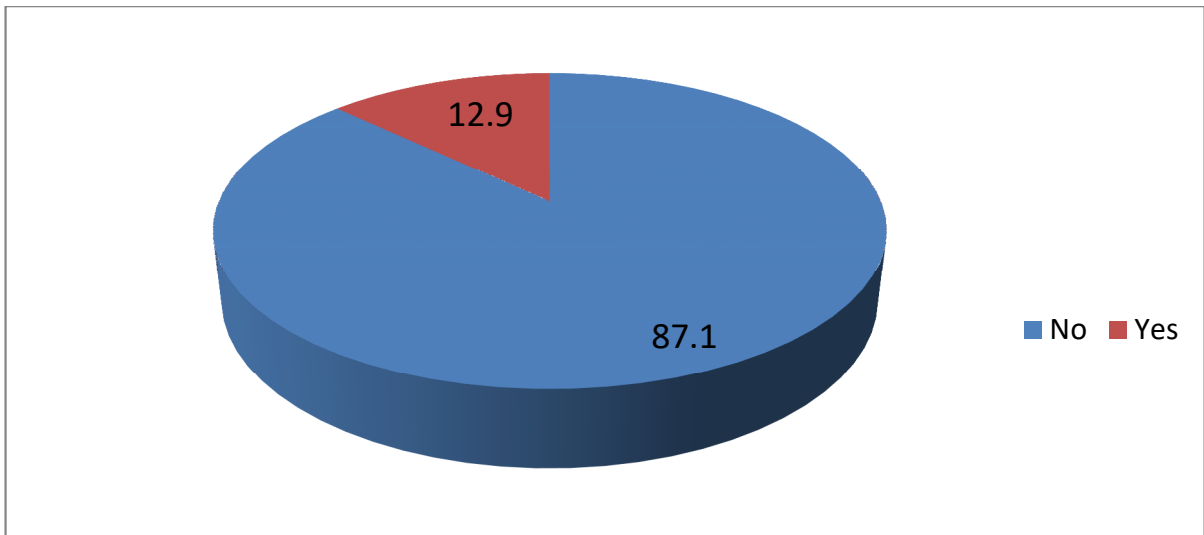


FIGURE 2: MAGNITUDE OF MAGNITUDE OF NON-VALVULAR ATRIAL FIBRILLATION AMONG HYPERTENSIVE PATIENTS AT SPHMMC, 2023.

In this study nearly half, 14(53.8%) and 16(61.5%) of hypertensive patients with NVAf have CHADS VASc score of 3 and HASBLED score 2 respectively. All patients with NVAf were on rate control treatment (Table 5).

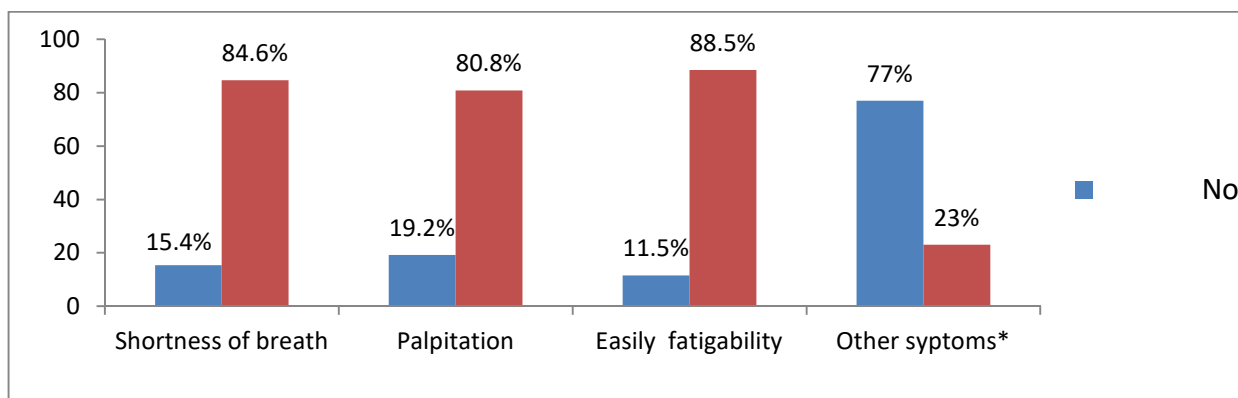
TABLE 4: CHARACTERISTICS OF NVAf PATIENTS AMONG HTN PATIENT AT SPHMMC, 2023(N=26)

Characteristics		Frequency	Perce nt
CHA2DS VASc score of patients with AF	1	1	3.8
	2	4	15.4
	3	14	53.8
	4	3	11.5
	5	4	15.4
HASBLED score of pts with AF	1	7	26.9
	2	16	61.5
	3	2	7.7
	4	1	3.8
NVAf patients started anticoagulation according to their CHADS2 VASc score	No	6	23
	Yes	20	77

CHADS VASc, HASBLED, NVAf→non-valvular atrial fibrillation

THE MAJORITY OF PATIENTS WITH NVAf WERE PRESENTED WITH SHORTNESS OF BREATH, PALPITATION, AND EASILY FATIGABILITY.

FIGURE 3: PRESENTING COMPLAINT OF AF PATIENT



Other symptoms: chest pain, stroke

Figure 3: Presenting symptoms of patients with NVAf among hypertensive patients at SPHMMC, 2023 (N=26)

5.5 Factors associated with NVAf:

In bivariable binary logistic regression analysis, gender, age, duration hypertension, end organ damage, LVH, BMI, having DM and dyslipidemia were eligible candidate variables to fit multivariable binary logistic regression analysis. However, in multivariable binary logistic regression analysis only age, LVH, DM and dyslipidemia were significantly associated with NVAf.

After adjusting all other variables, patients with age equal to fifty years or more were more than nine-fold (AOR: 8.6 (95%CI. (2.74, 26.91)) times increase the risk of NVAf compared with those with age less than 20-50. The odds of NVAf were more than four times (AOR: 4.74, 95% CI (1.32, 16.94) for hypertensive patients who had moderate and severe LVH compared with the counterparts. Similarly, hypertensive patients who had DM and dyslipidemia as a comorbidity were nearly eight (AOR: 8.23, 95% CI (2.75, 24.61)) and four (AOR: 3.84, 95% CI, (1.40, 10.53) times more likely to have NVAf compared with the counterparts respectively (**Table: 6**)

TABLE 5: BIVARIABLE AND MULTIVARIABLE ANALYSIS TO ASSESS FACTORS ASSOCIATED WITH NVAf AMONG HYPERTENSIVE PATIENT AT SPHMMC, 2023

Variable		Atrial fibrillation		COR (95% C.I)	AOR (95% C.I)	P
		Yes	No			
Gender	Female	17	101	1.38(0.58,3.27)	2.46 (.85,7.11)	.096
	Male	9	74	1	1	
Age	<50	14	149	1	1	
	≥50	12	26	4.91(2.04, 11.80)	8.6 (2.74, 26.91) *	0.001
Duration Of hypertension (years)	<5	8	60	1	1	
	5-10	10	64	1.17(0.43, 3.16)	.59 (.17, 2.070	.415
	>10	8	51	1.17(0.412(3.35)	.86 (.24, 3.052	.815
LVH	Yes	8	72	2.70 (1.16, 6.31)	4.74 (1.32, 16.94) *	.017
	No	14	92	1	1	
End organ damage	Yes	19	108	1.68(0.67, 4.21)	.71(.12, 3.97)	.702
	No	7	67	1	1	
BMI in kg/m ²	<25	72	8	1	1	
	≥25	103	18	1.57 (.64, 3.81)	1.15 (.37, 3.55)	.807
DM	Yes	11	21	5.37(2.18, 13.25)	8.23 (2.75, 24.61) *	.001
	No	15	154	1	1	
Dyslipidemia	Yes	15	50	3.40(1.46, 7.93)	3.84 (1.40, 10.53) *	.009
	No	11	125	1	1	

*Significant association, COR: crude odds ratio, AOR: adjusted odds ratio, CI: Confidence interval, P: significant value, BMI: Body Mass Index, and DM: Diabetes Mellitus.

CHAPTER SIX

6. Discussion

This study was conducted to assess the magnitude of non-valvular atrial fibrillation and associated factors among hypertensive patients at SPHMMC cardiac referral clinic to synthesis data in our set-up where only little is known about this significant public health problem.

In this study, the prevalence of non-valvular atrial fibrillation among hypertensive patients was 12.9% (95% CI: 8.5, 17.9). This finding was consistent the one done in Tanzania which was 10.25%[16] but higher than the one done in Senegal (5.35%) and Thailand (3.46%)[31].

Furthermore, our finding was higher than the population based studies which was conducted Jimma, Ethiopia and Sodo, Ethiopia which was 4.3%[42] and 0.43 % [20] respectively but as both are community based studies and were not exclusively on hypertensive patient but hypertension was one of the independent risk factor identified in both studies. On top of that our study set-up which is a tertiary hospital follows older patients and with multiple comorbidities is other explanation for the discrepancy.

Besides the study done in Tanzania which mentioned above there is no other study which evaluated the prevalence of AF in hypertensive patient as far as I know. But there are multiple evidence which shows the association of hypertension with AF in different prospective cohort and registry [5], [17], [27], [43].

In this study patients with age above 50 years old, LVH, having DM and dyslipidemia as comorbidities were independent risk factors which were significantly associated with NVAF.

Association between age and AF was established. The risk of AF increases at least 2 times for every decade above the age of 50'' years which was seen from study done in Germany[44], Framingham heart study cohort[17], global disease burden estimate 2010[5], global disease burden 2019[45]. The association between age and AF also seen Jimma and Sodo, Ethiopia[20 &33].

Other factor which found strongly associated in this study was hypertension related end organ damage (LVH) which was also demonstrated in different meta-analysis[46] and retrospective reviews done in Denmark[47] and Framingham heart study cohort[17] and study done in Tanzania LA enlargement which is surrogate marker for HHD(LVH) was associated with risk of AF[16].

Having diabetes mellitus (DM) was significantly associated with AF Framingham heart study cohort[17], study done in Germany[44], China[48], Switzerland[49].

Dyslipidemia was found to be associated with AF in our study even-though there are controversial data regarding the association between dyslipidemia and AF. A meta-analysis 6 observational cohort which was published on BMC in 2021 show that metabolic syndrome, where dyslipidemia is one component is a risk factor for AF but other confounding factors are

there[50]. The one which was done in Thailand after adjusting to other factor shows low LDL cholesterol associated with increased risk of AF[51]. An other studies from Beijing, China also demonstrate same findings[52].

Other important finding of this study was in 77% NVAf patient their CHA₂DS₂-VASc score was calculated and put on anticoagulation. The most common complaint of those patient with AF was short of breath, palpitation and easy fatigability which is consistent to the study done in Tanzania[25]. However, attributing these symptoms to AF is difficult as there are other confounding factors and was not assessed in those patients without AF. Blood pressure was controlled in 63.7% which is higher than other study done in Ghana which was 23.3% of patient achieve their blood pressure controlled [53] and meta-analysis which was done in Ethiopia to see the prevalence of uncontrolled HTN, found nearly half of HTN patient are uncontrolled[54]. Furthermore cross-sectional study done in Afghanistan on prevalence of uncontrolled HTN shows 77.3%. Although this may over or underestimate due the use only office blood pressure measurement.

6.2 Strength and limitations

6.2.1 Strength of the study

As far as I know this is the first focused research done on non-valvular AF in Ethiopia make it important input for further research on two common and increasing public health problem (HTN and AF). Besides as it was done in tertiary care center it is somewhat representative of the national disease burden as patients are referred here from most part of the country.

6.2.2 Limitation of the study

Even though this study provided crucial information about the prevalence of AF in patients with HTN and associated factors in Ethiopia and Sub-Saharan Africa where there is limited data about non valvular AF, it has limitation such as being done in a tertiary center where more advanced cases with multiple comorbidities have been followed, which may overestimate the result. As intermittent 12 lead ECG was made there is high chance of missing paroxysmal AF, which has similar complication as persistent or permanent AF. The other limitation is BP measurement was only done in office which is not the ideal way and misses masked HTN and may label white coat HTN as uncontrolled HTN. It is also single center cross-sectional study causality can't be inferred.

7. Conclusion and recommendation

7.1 Conclusion

In this study more than one-tenth (12.9%) of hypertensive patients had non-valvular atrial fibrillation. Elders with 50 years or more, LVH, and having DM and dyslipidemia as a comorbidity was significantly associated with NVAf.

7.2 Recommendations

More than 10% of our hypertensive patients at our referral clinic have AF which is significant number taking in mind the morbidity and mortality associated with it. It is very important to suspect AF in hypertensive especially in those age above 50 years, hypertension related end organ damage (LVH) and with comorbidities like DM and dyslipidemia. In our set-up at least pulse should check at every visit and 12-lead ECG probably good if it could be done at least Q 6-12 month particularly for those high-risk patients but it needs further study to see its cost-effectiveness and to determine best ways of screening.

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9. Annexes

9.1 ANNEX I: Information Sheet

Research Title: Assessing the magnitude of non-valvular atrial fibrillation and associated factors among hypertensive patient having active follow up at SPHMMC cardiac referral clinic. The primary reason for conducting this research is merely to synthesize knowledge on magnitude AF and associated factors on hypertensive patients and for subsequent plan of screening high risk patient to prevent the complications associated with AF. The ethical principles will be maintained throughout the study period and afterward by keeping the patient information anonymous and confidential.

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9.2 ANNEX II: Data Collection, structured questionnaire

Make circle (O) or write phrases or words where necessary

Magnitude of non-valvular AF in HTN patient at SPHMMC CRC

1. Demographics

- a. MRN -----
- b. Age -----
- c. Sex -----
- d. Occupation
- e. Marital status married -----single----- divorced ----- widowed
- f. Educational status a, formal-----b, informal-----

2. Physical characteristics

- g. Weight -----h. Height -----i. Waist circumference----j. BMI-----

4. Behavioral characteristics

- a. Significant smoking history
- b. Significant alcohol consumption
- c. Other illicit drug use----- specify-----

5. HTN

- a. SBP-----DBP-----
- b.PR---- i, regular----- ii, irregular-----
- c. Duration HTN I, <5yrs ii, 5-10 years, iii >10 years
- d. controlled ($\leq 140/80$, CKD & DM <130/80) e. Uncontrolled ($>140/80$)
- f. Treatment on

ACEI/ARBS-----CCB-----Thiazide diuretic, ----- BB-----, loop diuretics-----,
MRA----- other specify-----

6. HTN-related end organ damage

- a. HHD/IHD b. CKD

5. Other comorbidity

a. DM-----yes, no--- b. COPD---- yes-----no-----c. Thyrotoxicosis yes---, no----
d, dyslipidemia--- yes---no---

6. Lab characteristics mean $\pm$ SD

a. Creatinine -- b. eGFR (ml/min/1.73 m²)

g. UA

h. Proteinuria

7. ECG

a. AF--- YES----- NO-----

8. Echo

a. EF----

b. LVH—yes---- No-----

9. Patient current complaint complaint for AF patients

I, asymptomatic

II, symptomatic

a. SOB

b. Chest pain

c. Easy fatigability

d. Cough

e. Palpitation

f. Cough

g. Stroke

h. Other

10. AF patient----- CHADS2 VASc score-----HAS Bleed Score -----

a. Anticoagulation according to CHADS2 VASc score yes ----- No----

Other AF treatment a, rate control -----b, rhythm control----- c, none

9.3 ANNEX III: Assurance of Investigator

I the under signed resident agree to accept all responsibilities for the scientific, ethical and technical conduct of the research project and for provision of required progress reports as per terms and conditions of the Research and Publication Directorate and /or Department of Public Health of St. Paul's Hospital Millennium Medical College.

Name of the Resident: _____

Signature: _____

Date: _____

Approval of Advisors

Name of Public Health Advisor: Mir. Hanna Feleke (MPH)

Signature: - _____

Date: - _____

Name of Clinical Advisor: Dr. Esubalew Wooldeyes(MD, Internist, Consultant Cardiologist)

Signature: _____

Date: _____