

Prevalence, Clinical Features, and Associated Factors of Atrial Fibrillation Among Hypertensive Patients at Fort Portal Regional Referral Hospital, Uganda

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Background: Studies in various contexts have shown that atrial fibrillation (AF) among hypertensive patients varies in prevalence, clinical features, and associated factors. However, in Uganda, including Fort Portal Regional Referral Hospital (FPRRH), there is limited data on these aspects. This study assessed the prevalence, clinical features, and associated factors of AF among hypertensive patients attending FPRRH.

Methods: This hospital-based cross-sectional study was conducted at the medical outpatient clinic of FPRRH from October 2022 to January 2023. Hypertensive patients were consecutively enrolled during clinic visits. Data on sociodemographic, lifestyle, and clinical characteristics were collected. AF prevalence was calculated as the proportion of hypertensive patients diagnosed with AF, and logistic regression was used to identify associated factors. Variables with $p < 0.2$, odds ratios ≥ 2 or ≤ 0.5 , or biological plausibility were included in the multivariable model. Significance was set at $p < 0.05$. Data analysis was performed using Stata version 15.2.

Findings: Among 140 hypertensive patients, the prevalence of AF was 10% ($n = 14$). Most AF patients presented with fatigue (71.4%) and palpitations (71.4%), 28.6% reported syncope, while physical inactivity (29.3%). Physical inactivity (Adjusted Odds Ratio - AOR = 16.3, 95% CI: 2.15–64.30, $p = 0.007$) and abnormal pulse rates, low (AOR = 9.5, CI: 1.57–36.02, $p = 0.008$) and high (AOR = 8.7, CI: 2.21–25.09, $p = 0.007$), were significantly associated with AF.

Conclusion: The prevalence of AF at FPRRH was 10%, higher than in many regional studies. Fatigue and palpitations were the most common symptoms. Physical inactivity and abnormal pulse rates were key predictors. Routine screening, promotion of moderate physical activity, and early pulse monitoring are essential to reduce AF burden in hypertensive populations.

Keywords: atrial fibrillation, hypertension, prevalence, fatigue, palpitations

Introduction

Atrial fibrillation (AF) is a prevalent cardiac arrhythmia characterized by irregular electrical activity within the atria. It was first identified in human subjects through electrocardiograms (ECG) in 1906, with Rothberger and Winterberg linking it to absolute arrhythmia in 1909.¹ Hypertension, the leading cardiovascular condition globally, shares several risk factors with AF, such as diabetes, obesity, and aging.^{2,3} Chronic hypertension induces hemodynamic alterations and atrial remodeling, predisposing individuals to AF.⁴ Studies have consistently identified hypertension as a primary risk factor for AF development.⁵

The global burden of AF has been risen significantly, with an estimated 46.3 million individuals affected in 2016 compared to 33.5 million in 2010.⁶ Similarly, the prevalence of hypertension doubled from 648 million in 1990 to 1.28 billion in 2019.^{7,8} In sub-Saharan Africa, AF is underdiagnosed due to limited access to diagnostic tools such as ECGs, despite the high prevalence of hypertension.⁹ In Uganda, however, there is limited data on AF prevalence, clinical features, and associated factors, creating a significant knowledge gap.

Undiagnosed or poorly managed AF can lead to serious complications, including stroke, heart failure, and increased mortality among hypertensive patients and early detection is crucial for effective management and targeted intervention.^{10,11} Fort Portal Regional Referral Hospital (FPRRH), serves a mixed urban and rural population in western Uganda which provides a good setting to explore this issue due to its diverse patient base and access to outpatient chronic care.

This study aims to determine the prevalence, clinical features, and associated factors of atrial fibrillation among hypertensive patients attending FPRRH. Findings will help inform screening strategies, resource allocation, and clinical decision-makings.

Methodology

Study Design and Setting

This was a hospital-based cross-sectional analytical study conducted at the Hypertension Clinic of Fort Portal Regional Referral Hospital (FPRRH), a public tertiary hospital in Western Uganda serving six districts. The clinic operates on Mondays and Thursdays and is staffed by medical and senior house officers. The study was conducted between 27th October 2022 and 5th January 2023.

Study Population

The target population included hypertensive patients aged 18 years and above attending the hypertension clinic during the study period. Patients were consecutively enrolled at the point of care after getting informed written consent. The following were excluded from the study known cases of atrial fibrillation, patients with temporary or permanent pacemakers, those who were unconscious, or those below 18 years of age.

Sample Size Determination

A sample of 140 participants was determined using Kish Leslie's formula based on a 10.2% prevalence of AF among hypertensive patients in Tanzania,¹² with 95% confidence level and 5% margin of error.

$$n = \frac{Z_{\alpha/2}^2 * p(1 - p)}{d^2}$$

Where:

n = Sample size estimate of study participants.

$Z_{\alpha/2}$ = Standard Z value at 95% confidence interval, corresponding to 1.96

p = proportion of patients with AF, which is 10.2% in Tanzania¹²

d = the sampling error; 5%

$$n = \frac{1.96^2 * 0.102(1 - 0.102)}{0.05^2} = 140$$

Data Collection Procedures

Data were collected using structured questionnaires, physical examinations, and electrocardiograms (ECGs). The research team included the principal investigator and a trained nurse assistant. Sociodemographic and clinical data were collected via interview and review of patient records. Blood pressure was measured manually using a calibrated Yuwell aneroid sphygmomanometer. Readings were taken while seated after a 5-minute rest, with two values averaged. In Anthropometry, height and weight were measured using a stadiometer and weighing scale to calculate BMI. ECG recordings were performed using the EDAN SE-1 12-lead ECG machine. Electrodes were placed according to standard lead positions. AF was diagnosed based on criteria of AF, absence of P waves, presence of fibrillatory waves, and irregularly irregular R-R intervals.¹³ Physical activity was assessed using questions adapted from the World Health Organization's physical activity assessment tool and categorized as: physically active (≥ 30 minutes of moderate activity per day) and physically inactive (< 30 minutes per day) and recorded in the analysis as a binary variable (yes/no).^{14,15}

Data Quality Assurance

A pilot test was conducted at Kampala International University Teaching Hospital with 10 patients to validate the data collection tool which were not part of study analysis. Cronbach's alpha and the Content Validity Index (CVI) were used to confirm internal consistency and content validity. Research assistants received prior training and supervision to ensure protocol adherence. Data were reviewed daily for completeness and consistency before entry.

Data Management and Analysis

Data were entered in Excel 2016 and exported to Stata 15.2 for analysis. Descriptive statistics were used to summarize variables. AF prevalence was calculated as a percentage of hypertensive patients diagnosed with AF. Clinical features were presented as proportions among AF cases. Bivariate and multivariate logistic regression identified factors associated with AF. Variables with $p < 0.2$, crude ORs ≥ 2 or ≤ 0.5 , or biological plausibility were included in the final model. Statistical significance was set at $p < 0.05$.

Ethical Considerations

The study obtained ethical clearance from the Research Ethics Committee of Kampala International University (Reference: KIU-2022-158). Additional approval was granted by the administration of Fort Portal Regional Referral Hospital (FPRRH). Participation was voluntary and anonymized - patients were informed that they could withdraw at any time without affecting their care. All participants provided written informed consent before data collection. ECG results and relevant clinical findings were immediately shared with the attending physician for timely management. COVID-19 precautions were observed throughout the data collection period.

Results of the Study

Socio-Demographic and Lifestyle Characteristics of Participants

A total of 140 hypertensive patients were enrolled. The majority were female (57.9%), aged ≥ 55 years (54.3%, mean age = 54.5 ± 12.3), and resided in rural areas (62.8%). Regarding lifestyle, 70.7% reported engaging in physical activity, while 61.4% reported high salt intake. Alcohol consumption and smoking were uncommon, with 91.4% reporting no alcohol intake and 95.0% never smoked. The rest are shown in [Table 1](#).

Table 1 Socio-Demographic and Lifestyle Characteristics of Participants (N =140)

Characteristics		n(%)
Sex	Male	59 (42.1)
	Female	81 (57.9)
Age in years M=54.5, SD =12.3	<55	64(45.7)
	≥ 55	76 (54.3)
Formal education	None	45 (32.1)
	Primary	69 (49.3)
	$\geq$ Secondary	26 (18.6)
Occupation	Unemployed	124 (88.6)
	Employed	16 (11.4)
Residence	Rural	86 (62.8)
	Urban	54 (37.2)
Marital status	Single	8 (5.7)
	Married	104 (74.3)
	Widowed/divorced	28 (20.0)

(Continued)

Table 1 (Continued).

Characteristics		n(%)
Alcohol use	None	128 (91.4)
	Low	8 (5.7)
	Harmful	4 (2.9)
History of smoking	Never	133 (95.0)
	Abstainer	2 (1.4)
	Current smoker	5 (3.6)
Physical activity	Yes	99 (70.7)
	No	41 (29.3)
Salt intake	Adequate	18 (12.9)
	Low	36 (25.7)
	High	86 (61.4)

Abbreviation: M, Mean.

Medical Characteristics of Participants

Most participants had been on antihypertensive treatment for less than 5 months (64.3%) and had their BP checked within the past 6 months (90.7%). Over half were overweight (52.1%), and 94.3% had systolic blood pressure (SBP) ≥ 140 mmHg. Elevated diastolic blood pressure (DBP ≥ 90 mmHg) was noted in 89.3%. Abnormal pulse rates were observed in 27.2% of participants, with 23.6% having high pulse rates and 3.6% having low pulse rates and 33.6% had diabetes mellitus (DM) as the rest detailed in [Table 2](#)

Prevalence of Atrial Fibrillation

The overall prevalence of atrial fibrillation was 10.0% (n = 14, 95% CI: 5.97–16.27).

Table 2 Medical Characteristics of Participants

Characteristics		n(%)
Duration of HTN treatment(months)	<5	90 (64.3)
	≥ 5	50(35.7)
BP checkup in past 6 months	No	13 (9.3)
	Yes	127 (90.7)
History of stroke	No	112 (80.0)
	Yes	28 (20.0)
DM	No	93 (66.4)
	Yes	47 (33.6)
HIV	Negative	126 (90)
	Positive	14 (10)
BMI (kgs/m²)	Normal	51 (36.4)
	Underweight	3 (2.1)
	Overweight	73 (52.1)
	Obese	13 (9.3)
SBP	Normal (≤ 140 mmHg)	8(5.7)
	Elevated (≥ 140 mmHg)	132(94.3)
DBP	Normal (≤ 90 mmHg)	15(10.7)
	Elevated (≥ 90 mmHg)	125(89.3)
Pulse	Normal (60–100/min)	102 (72.9)
	High (> 100 /min)	33 (23.6)
	Low (< 60 /min)	5 (3.6)

Abbreviations: HTN, Hypertension, DM, Diabetes Mellitus, Body Mass Index, SBP, Systolic Blood Pressure. DBP, Diastolic Blood Pressure.

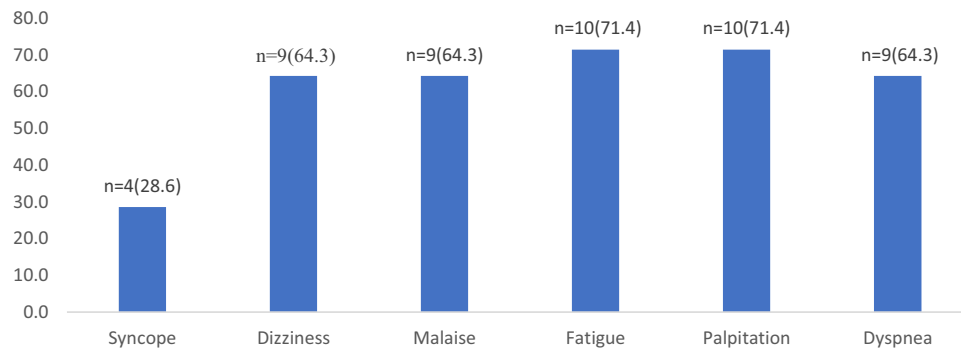


Figure 1 Clinical features of atrial fibrillation among patients with hypertension n=14.

Clinical Features of Atrial Fibrillation Among Patients with Hypertension

Among participants with AF (n = 14), the most common symptoms were fatigue (71.4%) and palpitations (71.4%). Syncope occurred in 28.6%. The details are in [Figure 1](#)

Bivariate Analysis of Factors Associated with Atrial Fibrillation Among Hypertensive Patients

Bivariate logistic regression identified several candidate variables with $p < 0.2$, crude odds ratio (COR) ≥ 2 or ≤ 0.5 . These included marital status, physical activity, duration of hypertension, HIV status, pulse rate, and symptoms such as palpitations, fatigue, malaise, dizziness, and syncope. Sex and age were included in multivariate analysis for their biological plausibility and to control confounding, despite not meeting statistical thresholds. The rest are detailed in [Table 3](#)

Table 3 Bivariate Analysis of Factors Associated with Atrial Fibrillation Among Hypertensive Patients

Factors		Atrial Fibrillation		COR (95%)	P
		Yes	No		
Sex	Male	7(11.9)	52(88.1)	1	0.532
	Female	7(8.6)	74(91.4)	0.7(0.23–2.12)	
Age	<55 years	6(9.38)	58(90.63)	1	0.821
	≥55 years	10.5(8.3)	68(89.5)	1.1(0.37–3.47)	
Education	None	4(8.9)	41(91.1)	1	0.646
	Primary	8(11.6)	61(88.4)	1.3(0.38–4.76)	
	≥Secondary	2(7.7)	24(92.3)	0.9(0.15–5.02)	
Occupation	Unemployed	13(10.5)	111(89.5)	1.8(0.21–14.1)	0.600
	Employed	1(6.3)	15(93.7)	1	
Residence	Rural	7(8.1)	79(91.9)	1	0.486
	Urban	6(11.8)	45(88.2)	1.5(0.48–4.75)	
Marital Status	Single	1(12.5)	7(87.5)	1	0.935
	Married	12(11.5)	92(88.5)	0.9(0.10–8.08)	
	Widowed/divorced	1(3.6)	27(96.4)	0.3(0.01–4.68)	
Alcohol use	No	13(10.2)	115(89.8)	–	0.39
	Low	0(0.0)	8(100.0)	–	
	Harmful	1(25.0)	3(75.0)	–	
Smoking	Never	13(9.8)	120(90.2)	–	0.68
	Abstainer	0(0.0)	2(100.0)	–	
	Smoker	1(20.0)	4(80.0)	–	

(Continued)

Table 3 (Continued).

Factors		Atrial Fibrillation		COR (95%)	P
		Yes	No		
Physical activity	Yes	5(5.1)	94(94.9)	—	0.005*
	No	9(22.0)	32(78.0)	5.2(1.65–16.94)	
Salt intake	Adequate	2(11.1)	16(88.9)	1	0.741
	Low	3(8.3)	33(91.7)	0.7(0.11–4.80)	
	High	9(10.5)	77(89.5)	0.9(0.18–4.74)	
Treatment for HTN period(months)	<5	7(7.8)	83(92.2)	1	0.246
	≥5	7(14.0)	43(86.8)	1.9(0.64–5.86)	
BP check	No	1(7.7)	12(92.3)	1	0.772
	Yes	13(10.2)	114(89.8)	1.4(0.16–11.39)	
Stroke	No	10(8.9)	102(91.1)	1	0.402
	Yes	4(14.3)	24(85.7)	1.7(0.49–5.89)	
DM	No	9(9.7)	84(90.3)	1	0.498
	Yes	5(10.6)	42(89.4)	1.5(0.47–4.69)	
HIV	No	12(9.5)	114(90.5)	1	0.06
	Yes	2(14.3)	12(85.7)	1.6(0.32–7.93)	
SBP	Normal	1(12.5)	7(87.5)	1	0.809
	Elevated	13(9.9)	119(90.1)	0.8(0.09–6.71)	
DBP	Normal	2(13.3)	13(86.7)	1	0.650
	Elevated	12(9.6)	113(90.4)	0.7(0.14–3.43)	
Pulse	Normal (60–100)	4(3.9)	98(96.1)	1	0.001
	High (>100)	9(27.3)	24(72.7)	9.2(2.61–32.38)	
	Low (<60)	1(20.0)	4(80.0)	6.1(0.55–68.10)	
BMI	Normal	7(13.7)	44(86.3)	—	0.46
	Underweight	0(0.0)	3(100.0)	—	
	Overweight	7(10.6)	66(78.9)	—	
	Obese	0(0.0)	13(100.0)	—	
Dyspnoea	No	5(8.8)	57(80.5)	1	0.498
	Yes	9(13.0)	69(87.0)	1.5(0.47–4.69)	
Palpitations	No	4(6.5)	59(93.5)	1	0.202
	Yes	10(13.0)	67(87.0)	2.2(0.65–7.39)	
Fatigue	No	4(6.5)	58(93.5)	1	0.212
	Yes	10(13.0)	67(87.0)	2.2(0.64–7.27)	
Malaise	No	5(6.8)	68(93.2)	1	0.202
	Yes	9(13.4)	58(86.6)	2.1(0.67–6.65)	
Dizziness	No	5(6.9)	67(93.1)	1	0.201
	Yes	9(13.6)	57(86.4)	2.1(0.67–6.67)	
Syncope	No	10(9.3)	97(90.7)	1	0.565
	Yes	4(12.9)	27(87.1)	1.4(0.42–4.94)	

Note: * $p < 0.05$.

Abbreviations: HTN, Hypertension, BP, Blood Pressure DM, Diabetes Mellitus, Body Mass Index, SBP, Systolic Blood Pressure. DBP, Diastolic Blood Pressure.

Multivariate Analysis of Factors Associated with Atrial Fibrillation Among Hypertensive Patients

In the multivariate logistic regression model, lack of physical activity remained significantly associated with AF (AOR = 6.3, 95% CI: 2.15–24.30, $p = 0.007$). Abnormal pulse rates also showed strong associations: high pulse (>100 bpm; AOR = 8.7, 95% CI: 2.21–25.09, $p = 0.007$) and low pulse (<60 bpm; AOR = 9.5, 95% CI: 1.57–36.02, $p = 0.008$). The rest is detailed in Table 4

Table 4 Multivariate Analysis of Factors Associated with Atrial Fibrillation Among Hypertensive Patients

Factors		Atrial Fibrillation		AOR (95%)	P
		Yes	No		
Sex	Male	7(11.9)	52(88.1)	1.0	0.668
	Female	7(8.6)	74(91.4)	1.5(0.22–10.90)	
Age	<65 years	12(10.4)	103(89.6)	1.0	0.883
	≥65 years	2(8.3)	22(91.7)	0.8(0.04–16.66)	
Marital Status	Single	1(12.5)	7(87.5)	1.0	0.943
	Married	12(11.5)	92(88.5)	0.9(0.05–14.98)	
	Widowed/divorced	1(3.6)	27(96.4)	0.1(0.00–3.05)	
Physical activity	Yes	5(5.1)	94(94.9)	1.0	0.007**
	No	9(22.0)	32(78.0)	6.3(2.15–24.30)	
Treatment for HTN period(months)	≤5	9(8.1)	102(91.9)	1.0	0.444
	>5	5(17.2)	24(82.8)	2.8(0.21–37.03)	
HIV	No	12(9.5)	114(90.5)	1.0	0.655
	Yes	2(14.3)	12(85.7)	1.3(0.09–4.50)	
Pulse	Normal (60–100)	4(3.9)	98(96.1)		0.007**
	High (>100)	9(27.3)	24(72.7)	8.7(2.21–25.09)	
	Low (<60)	1(20.0)	4(80.0)	9.5(1.57–36.02)	
Palpitations	No	4(6.5)	59(93.5)	0.1	0.078
	Yes	10(13.0)	67(87.0)	6.6(0.81–54.19)	
Fatigue	No	4(6.5)	58(93.5)	1.0	0.855
	Yes	10(13.0)	67(87.0)	0.8(0.08–7.94)	
Malaise	No	5(6.8)	68(93.2)	1.0	0.547
	Yes	9(13.4)	58(86.6)	0.8(0.08–7.94)	
Dizziness	No	5(6.9)	67(93.1)	1.0	0.083
	Yes	9(13.6)	57(86.4)	7.6(0.77–75.72)	
Syncope	No	10(9.3)	97(90.7)	1.0	0.655
	Yes	4(12.9)	27(87.1)	0.6(0.09–4.50)	

Note: **p <0.01, HTN: Hypertension.

Discussion

This study aimed to determine the prevalence, clinical features and associated factors of atrial fibrillation (AF) among hypertensive patients at Fort Portal Regional Referral Hospital (FPRRH).

Prevalence of AF Among Hypertensive Patients

The observed AF prevalence was 10%, which is similar to prevalence reported in other sub-Saharan African settings, including a study at the Jakaya Kikwete Cardiac Institute in Tanzania that found a prevalence of 10.2% which involved 391 patients of having hypertension.¹² Although our prevalence is comparable, it is substantially higher than that reported in parts of Asia. For instance, a cross-sectional study in Thailand reported a lower prevalence of 3.46%.¹⁶ Conversely, prevalences in high-income countries such as Switzerland (19.5% of 97 patients) and Germany (31.1% of 225 patients) are much higher compared to our study.^{17,18} These discrepancies may reflect differences in population age, diagnostic capacity, and screening practices. Lower prevalence rates in developing countries may also stem from underdiagnosis due to limited ECG access, shorter life expectancy, or differences in healthcare-seeking behavior.¹⁹

Clinical Features of Atrial Fibrillation Among Patients with Hypertension

Among participants diagnosed with AF, the most commonly reported symptoms were fatigue and palpitations (both 71.4%), with syncope being less frequent (28.6%). These findings are consistent with prior studies from Cameroon and Tanzania, which also identified palpitations and easy fatigability as common AF symptoms.^{12,20} The similarity across studies supports the typical clinical presentation of AF even in resource-limited settings.

Factors Associated with Atrial Fibrillation Among Hypertensive Patients

Multivariate analysis in our study found that non-participation in physical activity and abnormal pulse rates (either high or low) was significantly associated with AF. Patients who did not engage in physical activity were 6.3 times more likely to have AF (AOR = 6.3, $p = 0.007$), while those with high and low pulse rates had adjusted odds ratios of 8.7 $p = 0.007$ and 9.5 $p = 0.008$, respectively. Our findings on physical inactivity align with other literature linking sedentary behavior to elevated AF risk. A cohort study conducted in Sweden by Drca et al found that higher levels of leisure-time physical activity, including walking and bicycling, were associated with a reduced risk of atrial fibrillation.²¹ However, studies in high-income country showed a U-shaped relationship, where both low and very high levels of physical activity may increase AF risk.^{22,23} In our study, physical activity was self-reported and categorized based on duration as either <30 minutes or ≥ 30 minutes of moderate activity per day. Adults with hypertension and AF are encouraged to have a moderate physical activity, which has been shown to improve cardiorespiratory fitness and with lower risk of AF.²⁴ These findings reinforce the value of encouraging moderate physical activity among hypertensive patients as a practical strategy to reduce AF risk.

From a pathophysiological perspective, vigorous or prolonged endurance activity may induce atrial stretch, fibrosis, inflammation, and autonomic imbalance creating a susceptibility for AF onset. While moderate physical activity reduces sympathetic tone, improves blood pressure control, and enhances cardiorespiratory fitness, thereby protection against AF.²⁵

Abnormal pulse rate, both low and high were independently associated with AF in our study. This finding is consistent with results from the Kangwon National University Holter registry in South Korea, which identified both low and high heart rates as predictors of AF among hypertensive patients.²⁶ Bradycardia may reflect underlying sinus node dysfunction or increased vagal tone, leading to atrial ectopy. Conversely, tachycardia may indicate increased sympathetic drive or unrecognized paroxysmal AF, both of which promote atrial remodeling and arrhythmogenesis.^{27,28}

These pathophysiological insights emphasize that pulse rate abnormalities are not merely markers but potentially modifiable risk factors in AF, particularly among hypertensive populations.

AF and coronary artery disease (CAD) frequently coexist and share common risk factors, including diabetes mellitus (DM), hypertension, advancing age, dyslipidemia, obesity, smoking, and physical inactivity.^{29,30} An integrative review by Batta et al highlights a reciprocal - vicious cycle - in which CAD promotes AF through atrial ischemia, inflammation, and fibrosis that disrupt cardiac conduction. On the other hand, AF contributes to CAD progression by inducing endothelial dysfunction and systemic inflammation which may accelerate atherosclerosis and result in CAD.³⁰ In hypertensive patients already at elevated cardiovascular risk, this overlap warrants attention. Routine assessment for CAD in patients diagnosed with AF (and vice versa) could support more comprehensive cardiovascular care and timely therapeutic interventions.

Study Limitations

The sample size was modest, which may limit the generalizability of the findings to other hypertensive populations. Due to the cross-sectional design, it was not possible to establish causal relationships between associated factors and atrial fibrillation. Physical activity was assessed through self-report. The use of a single resting ECG could have led to underdiagnosis of paroxysmal or intermittent AF. Furthermore, the study did not assess potentially important clinical covariates such as thyroid function, echocardiographic findings which may have influenced the observed associations.

Conclusions

This study found a 10% prevalence of atrial fibrillation (AF) among hypertensive patients at FPRRH. AF was significantly associated with physical inactivity and abnormal pulse rates, including both tachycardia and bradycardia. These findings underscore the importance of routine ECG screening in hypertensive populations, particularly among sedentary individuals and those with irregular heart rates. Encouraging moderate physical activity and regular pulse monitoring may support early identification and better management of AF, especially in resource-limited settings where underdiagnosis is common. Further longitudinal studies are warranted to validate these associations and inform targeted interventions.

Data Sharing Statement

Data can be obtained upon request from author the corresponding author (Yahye Mohamed Jama, email: jama.yahye@studwc.kiu.ac.ug).

Ethical Approval and Consent to Participate

Ethics approval and consent to participate of the study was approved by Kampala International University - Research ethics committee (Ref no: KIU-2022-158). The study complies with Helsinki declaration.

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Disclosure

The authors declare that they have no conflicts of interest.

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