# Cardiovascular Disease Risk Factors and Arrhythmia Burden in Hypertensive Women: A Cross-sectional Study in a Semi-urban African Community.

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## Background

2.

Cardiovascular disease (CVD) is a leading cause of death in women. Systemic hypertension is the commonest risk factor for CVD, and it frequently coexists with other risk factors in women, thereby increasing the absolute cardiovascular risk.

## Objective

*This study set out to study the spectrum of arrhythmia burden and CVD risk factors among hypertensive women. Method* 

This is a cross-sectional study involving 300 hypertensive women and 150 age and sex-matched normotensive women as controls. Participants that met the inclusion criteria were recruited consecutively into the study. Prevalence and pattern of cardiovascular disease risk factors were sought by taking relevant history and examination. Blood was collected for glucose and lipid estimation. Patients underwent 24-hour Holter electrocardiography (ECG) and resting ECG study. Data were analysed using Statistical Package for Social Sciences (SPSS version 17.0 Chicago Illinois) software.

## Results

The mean age of both groups was similar  $(57.15\pm11.58$  years for hypertension group and  $56.83\pm13.41$  years for controls; p = 0.3967). The prevalence of generalized obesity was significantly higher in the hypertension group, as compared with controls (37.3% vs 22%, p=0.001). The overall prevalence of hypercholesterolemia was significantly higher in the hypertension group (12.33%), compared with controls (4%). 24-hour Holter ECG showed that 176 (59.7%) patients in the hypertension group and 50 (33.3%) control subjects had arrhythmia, with premature ventricular complex being the commonest arrhythmic pattern.

#### Conclusion

CVD risk factors and ventricular arrhythmia are more common in women with hypertension. Early risk factor detection and management in hypertensive women is desirable.

Keywords: hypertension, risk factors, cardiovascular disease, women

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## I. Introduction

There is emerging evidence showing that the pattern of diseases in sub-Saharan Africa is changing, with cardiovascular disease alone accounting for 9.2% of the total mortality [World Health Organization (WHO) 2002]<sup>1</sup>. Systemic hypertension is a major public health problem<sup>2</sup>. It is the most frequent risk factor for cardiovascular disease, and frequently coexists with other risk factors, thereby increasing the absolute cardiovascular risk<sup>3</sup>.

Cardiovascular diseases have been described primarily as a 'male disease', and evidence-based clinical standards have been created on male patho-physiology and outcomes<sup>4</sup>. As a result, women are often misdiagnosed or under-diagnosed<sup>4</sup>.

Risk factors for cardiovascular disease in women may be modifiable or non- modifiable. Modifiable cardiovascular risk factors include systemic hypertension, type-2 diabetes mellitus (T2DM), dyslipidaemia, obesity, cigarette smoking, metabolic syndrome, lifestyle (lack of exercise, alcohol abuse and dietary habits) and psychosocial factors. Non-modifiable cardiovascular risk factors are age, gender, family history and post-menopausal state.

Arrhythmia is a common co-morbidity in patients with systemic hypertension and a manifestation of hypertensive heart disease. Underlying mechanisms are many, including left ventricular hypertrophy (LVH), myocardial ischaemia, impaired left ventricular function and left atrial enlargement. Any form of arrhythmia may be associated with LVH but ventricular arrhythmia is more common and could be life-threatening<sup>5</sup>. Adebayo et al<sup>6</sup> in a study on 'Evaluation of Indications and Arrhythmic Pattern of 24-hour Holter ECG among Hypertensive and Diabetic patients at Ile-Ife, Nigeria' reported palpitation as the commonest indication and premature ventricular contraction as the commonest arrhythmic pattern. The Atherosclerosis Risk in Communities (ARIC) study<sup>7</sup> of more than 15,000 African American and White men and women reported that hypertension is associated with frequent or complex ventricular ectopic beats. Omotoso et al<sup>8</sup> studied arrhythmias in 2017 Nigerian hypertensive heart disease patients and reported that premature ventricular commonest arrhythmic pattern.

Only about 55% of women identified CVD as their greatest health risk in a 2006 survey conducted by the American Heart Association (AHA)<sup>9</sup> despite estimates that a 40-year old woman has a lifetime risk of CVD of 32%<sup>10</sup>. Studies over the last several decades from United States<sup>11</sup> also indicate that despite an overall reduction in the death rate due to CVD, the rate of decline is less for women than men, and less for African- American women than White women. This suggests that women have little insight into their own risk of heart disease<sup>9</sup>. Women also have a heightened mortality burden from cardiovascular disease than men<sup>11</sup>.

## 1.1 What is already known:

Cardiovascular disease in women has to date, largely been under-recognized, under-diagnosed and under-treated and there are few data on the burden of cardiovascular disease risk factors in hypertensive women in Nigeria. However, cardiovascular disease is a leading cause of death in women around the world<sup>12</sup>.

## **1.2 What this research adds:**

The findings from this study are envisaged to elucidate CVD risk factors in hypertensive women, this will help to improve early detection, prompt diagnosis and treatment of these risk factors. Secondarily, it may promote advocacy and tools such as prevention campaigns that utilize understanding of gender to encourage heart-healthy behaviours and target risk behaviour.

## II. Aim

The overall aim of this study is to determine the prevalence and pattern of cardiovascular disease risk factors associated with systemic hypertension in women. The occurrence and characterization of arrhythmias using resting electrocardiography (ECG) and 24-hour Holter ECG in hypertensive women will also be assessed.

## III. Methods

**3.1 STUDY LOCATION:** The study was carried out at Obafemi Awolowo University Teaching Hospitals Complex (OAUTHC), Ile-Ife, Nigeria. Ile-Ife is a semi-urban ancient Yoruba city in Osun State, South-Western Nigeria

**3.2 STUDY POPULATION**: This consisted of hypertensive women presenting at Cardiac Care Unit and Adult Accident and Emergency (A/E) unit of OAUTHC who satisfied the inclusion criteria.

**3.3 STUDY DESIGN:** This is a cross-sectional study involving hypertensive women with age and sex-matched normotensive women as control. Prevalence and pattern of cardiovascular disease risk factors was sought by taking relevant history with the use of interviewer administered proforma and physical examination including weight, height and office blood pressure measurement. Blood was collected for fasting blood glucose and 2-hour postprandial blood sugar, fasting lipid profile, packed cell volume, electrolytes, urea and creatinine. Patients underwent electrophysiological studies which include 24-hour Holter electrocardiography (ECG) and resting ECG.

**3.4 SAMPLING TECHNIQUE:** Subjects that fulfilled the inclusion criteria (aged 18-75 years) were consecutively recruited for this study until sample size is met. The control subjects were apparently healthy age and sex-matched volunteers with normal blood pressure recruited from among patients' relatives, hospital staff members, medical students, and Ile-Ife community dwellers who responded to adverts placed at strategic positions within the hospital calling for research volunteers.

#### **3.5 SAMPLE SIZE DETERMINATION**

The sample size was determined using the formula<sup>13</sup>.

$$N = \frac{(Zi-a)^2 P(1-P)}{d^2}$$

N= Minimum sample size.

a= Significant level/degree of effort tolerable for this study at 0.05 confidence level = 95%. Zi - a = 1.96 (from Z table)

P= best estimate of prevalence of hypertension in women from literature review =  $25.4\%^{14}$ .

d= absolute precision of 5%

$$N = \frac{1.96^2 \times 0.254 (1-0.254)}{0.05^2}$$

= 291.2

The estimated sample size of 291.2 was calculated. To accommodate for the dropouts from the study (approximately 3% drop-out rate), the sample size was made up to 300.

Therefore, a total of 300 hypertensive women and 150 age and sex-matched apparently healthy normotensive women were recruited for this study.

## **3.6 INCLUSION CRITERIA**

Women aged 18-75 years with systemic hypertension according to the WHO protocol<sup>15</sup> or previously diagnosed hypertensive on medications.

## **3.7 EXCLUSION CRITERIA**

Known type 2 diabetes mellitus patients. Pregnant women.

## **3.8 ETHICAL CONSIDERATION**

Approval of the Ethics and Research Committee of the OAUTHC was sought and obtained before the commencement of the study.

Informed consent of the individuals for the study were obtained verbally and in written form.

## 3.9 DATA COLLECTION- This was carried out as follows:

#### **3.9.1 PROTOCOL 1: HISTORY AND EXAMINATION**

Data were obtained from participants using interviewer administered proforma and physical examination conducted by the investigator. Information on smoking habits, alcohol use, dietary habits, age at menopause, physical activity and family history of hypertension was recorded. Smoking was considered present if subjects reported smoking up to the day of the interview. Alcohol intake was calculated as the percentage of alcohol multiplied by volume (milliliter), divided by 1000. Low risk alcohol consumption was defined as a maximum of 3 units per day in females, with at least 2 days per week free of alcohol consumption; higher consumption was considered high risk<sup>16</sup>.

#### 3.9.2 PROTOCOL 2: BP MEASUREMENT

All participants had their blood pressure (BP) measured by the researcher only. BP was measured in the office using the left arm in the sitting position (after resting for 10 minutes) with mercury sphygmomanometer using standard procedures. The systolic BP was recorded at phase I Korokoff sounds while the diastolic BP was recorded at phase V Korokoff sounds. Hypertension was defined as a systolic BP  $\geq$ 140mmHg and/or diastolic BP  $\geq$ 90mmHg or the current use of anti-hypertensive medications.

#### 3.9.3 PROTOCOL 3: ANTHROPOMETRIC MEASUREMENT

Anthropometric data was obtained by standard methods. Weight was taken with light clothing on with a weighing scale and measured to the nearest gram. A stadiometer was used for measurement of height. Body mass index (BMI) was calculated as weight in kilograms (kg), divided by the square of height in meters ( $m^2$ ).

The waist and hip circumference were measured using the standard methods.

Obesity or overweight was defined using the WHO criteria<sup>17</sup>. WHO Classification of Obesity in Adults using BMI

who Classification of Obesity II	
Underweight	<18.5kg/m <sup>2</sup>
Normal weight	18.5- 24.9 kg/m <sup>2</sup>
Overweight	$25-29.9 \text{ kg/m}^2$
Class I or Mild Obesity	$30-34.9 \text{ kg/m}^2$
Class II or Severe Obesity	35- 39.9 kg/m <sup>2</sup>
Class III or Extreme Obesity	$\geq 40 \text{ kg/m}^2$

**3.9.4 PROTOCOL 4: ELECTROCARDIOGRAPHY (ECG)** - A conventional resting 12-lead ECG was performed. The recommendation of the American Heart Association (AHA) concerning standardization of leads and specification for instrument were followed<sup>18-19</sup>. The 12-lead resting electrocardiogram (ECG) of the patient was obtained with the aid of a 3-channel electrocardiograph (Cardiofax YD-907D). The ECG was done with the machine set at standards with a paper speed of 25mm/s and amplitude of 10mm/mV. Lead II was used for long rhythm strip recording and evaluation.

The ECG was analyzed to obtain the occurrence and pattern of arrhythmia.

**3.9.5 PROTOCOL 5: 24-hour Holter ECG Monitoring:** A 24-hour ambulatory Holter ECG was recorded using the Schiller type (MT-101) with a bipolar V1-V5 lead system. Patients were thoroughly educated about the test and handling of the recorder. The Holter monitor was strapped to the patient's waist with the channel leads appropriately placed on the chest<sup>20</sup>. Patients were asked to go home, continue their normal activities and record timing of any symptoms. After completion of the recording over a 24-hour period, the recorder was retrieved and analyzed with Schiller's Cardiovit CS-200 digital ECG computer. The following data was recorded: heart rhythm, heart rate, heart rate variability and arrhythmias (multiple ventricular ectopic, ventricular tachycardia, premature atrial complexes, supraventricular tachycardia and atrial fibrillation).

## 3.9.6 PROTOCOL 6: LABORATORY TESTS

**I. FASTING BLOOD GLUCOSE AND 2-HOUR POST-PRANDIAL:** After 10-12 hours of overnight fast, venous blood was obtained from the subjects and analyzed for the fasting blood glucose. A second sample was collected 2 hours post-prandial for blood sugar measurement. All samples were quickly sent to Chemical Pathology unit and analyzed immediately using the glucose oxidase method. Diabetes mellitus and impaired fasting glucose was diagnosed according to the WHO criteria<sup>21</sup>.

**II. FASTING LIPID PROFILE**: After 10-12 hours of overnight fast, venous blood was centrifuged and the serum immediately separated and the concentrations of triglycerides (TG), total cholesterol (TC) and its fractions [LDL-C, HDL-C] were ascertained. The atherogenic Index of plasma (TC/HDL-C and LDL/HDL-C) was calculated. For the purpose of this study, the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) cut off points was used to identify subjects with desirable, borderline high and high levels of lipoprotein risk factors<sup>22</sup>. Electrolytes, packed cell volume (PCV) and creatinine are also estimated.

#### 3.10DATA ANALYSIS

Data were analysed using Statistical Package for Social Sciences (SPSS version 17.0 Chicago Illinois) software. Data were represented using descriptive statistics such as tables and bar charts where appropriate. Categorical variables were expressed as proportions and percentages while continuous variables were expressed as means and standard deviation Differences between 2 continuous variables were determined with the independent student t-test. Level of significance is P-value of  $\leq 0.05$  and a confidence interval of 95% was used.

#### **IV. Results**

Three hundred (300) hypertensive women and one hundred and fifty (150) normotensive control subjects were consecutively recruited over the study period.

### 4.1 Demography and Clinical Characteristics of the Study Population

The demographic and clinical characteristics of the study population are shown in Table 1. The mean age of both groups was similar,  $(57.2\pm11.6 \text{ years}$  for hypertension group and  $56.8\pm13.4 \text{ years}$  for controls; p = 0.3967). The mean duration of hypertension in the hypertension group was  $5.6\pm6.7$  years while the mean age at menopause of the study population was  $50.5\pm2.7$  years. The systemic hypertension group had significantly higher mean BMI ( $28.50\pm5.70 \text{ kg/m}^2$  for hypertension group and  $25.57\pm3.70\text{kg/m}^2$  for controls, p=0.001). The mean values of other variables including weight, waist circumference, waist-hip ratio, heart rate at rest, pressure-rate product at rest, systolic and diastolic blood pressure at rest were also significantly higher in the hypertension group. Family history of hypertension was detected in 87(29%) hypertensive patients and 29 subjects (9.66\%) for the control group.

Table 1: Demographic and Chinical Characteristics of the Study Population				
Parameter	HTN Subjects	Control	P value	
Sex: Females (n)	300	150		
Mean±SDMean±SD				
Age (years)	$57.15 \pm 11.58$	56.83±13.41	0.3967	
Weight (kg)	72.35±15.24	67.38±10.55	0.0002	
Height (meters)	$1.59 \pm 0.06$	$1.62 \pm 0.05$	0.7933	
BMI (kg/m <sup>2</sup> )	$28.50\pm5.70$	25.57±3.70	0.001	
BSA (m <sup>2</sup> )	$1.78 \pm 0.20$	$1.74 \pm 0.15$	0.0113	
Waist Circ (cm)	90.59±14.61	84.43±10.75	0.001	
Hip Circ (cm)	99.83±11.55	95.57±8.10	0.001	
Waist/Hip Ratio	$0.91 \pm 0.08$	$0.88 \pm 0.05$	0.0007	
HRrest (b/min)	78.22±11.43	$71.84 \pm 8.18$	0.001	
SBPrest (mmHg)	$138.89 \pm 23.50$	120.80±10.53	0.001	
DBPrest (mmHg)	84.91±13.75	75.35±8.74	0.001	
MAPrest (mmHg)	$102.88 \pm 15.57$	90.50±7.42	0.001	
PRPrest (mmHg/min	<b>x 10<sup>-2</sup>)</b> 108.39±23.11	86.78±12.44	0.001	
FH of HTN	87 (29)	29(9.66)	0.027	

**KEY: BMI**= Body mass Index; **BSA**= Body surface area, **HRrest=** Heart rate at rest; **SBPrest=** Systolic blood pressure at rest; **DBPrest=** Diastolic blood pressure at rest; **MAPrest=** Mean arterial pressure at rest;**PRPrest=** Pressure-rate product at rest; **FH of HTN**= Family history of hypertension, Circ= Circumference.

## 4.2 Laboratory Findings of the Study Population

Table 2 shows the laboratory findings of the study population. The mean serum creatinine, total cholesterol, triglycerides, LDL-C and FBG were significantly higher in the hypertension group compared with controls. The systemic hypertension group had significantly lower mean PCV ( $38.55\pm3.14\%$  for hypertension group and  $39.59\pm2.26\%$  for controls, p=0.0002) and serum sodium compared with control group. Sub-analysis of the hypertension group showed that hypertensive heart failure (HHF) patients had significantly lower PCV ( $37.40\pm4.18\%$  vs  $38.95\pm2.58\%$ , P=0.001) and lower sodium ( $132.73\pm3.88$ mmol/L vs  $136.04\pm3.32$ mmol/L, P=0.001), as compared with hypertension without heart failure sub-group. The HDL-C and serum urea were higher in control group, though this difference was not statistically significant.

Parameter	HTN Subjects	Control	P value
PCV (%)	38.55±3.14	39.59±2.26	0.001
Sodium (mmol/L)	135.19±3.75	138.61±2.63	0.001
Potassium (mmol/L)	4.06±0.46	$4.19 \pm 0.48$	0.7884
Creatinine (nmol/L)	94.79±28.84	79.60±13.23	3 0.001
Urea (mmol/L)	$4.22 \pm 0.45$	4.05±0.76	0.9773
TC (mmol/L)	5.03±2.83	3.49±0.83	0.001
TG (mmol/L)	$2.24\pm0.64$	$1.07 \pm 0.44$	0.001
LDL-C (mmol/L)	$3.20\pm2.30$	$1.53 \pm 1.08$	0.001
HDL-C (mmol/L)	$1.47 \pm 0.76$	$1.54\pm0.31$	0.8819
FBG (mmol/L)	4.97±0.76	$4.14 \pm 1.04$	0.001
2HPP (mmol/L)	6.41±1.28	6.37±1.23	0.3777
TC/ HDL	3.29±1.85	2.38±0.89	0.001
LDL/HDL	2.16±2.01	1.09±1.05	0.001

**KEY: HTN=** hypertension, **PCV=** Packed cell volume; **TC=** Total cholesterol; **TG=** Triglycerides; **LDL-C=** Low density lipoprotein cholesterol; **HDL-C=** High density lipoprotein cholesterol; **FBG=** Fasting blood glucose; **2HPP=** 2-hours post-prandial.

Figure 1 is a bar chart showing mean atherogenic index (using TC/HDL-C and LDL-C/HDL-C) in both study groups. The hypertension group had significantly higher mean TC/HDL-C (3.29±1.85 for hypertension group



and 2.38±0.89 for controls, p=0.001) and LDL-C/HDL-C (2.16±2.01 for hypertension group and 1.09±1.05 for controls, p=0.001)

Figure 1 is a bar chart showing mean atherogenic index of plasma (using TC/HDL-C and LDL-C/HDL-C) in both study groups. Key: HTN= hypertensive patient group.

The prevalence of generalized obesity was significantly higher in the hypertension group, as compared with controls (37.3% vs 22%, p=0.001). Fifty-two-point three percent of the hypertension group had truncal obesity as compared to 30% of the control group. There was no statistical difference between the prevalence of IFG/DM in both groups. The overall prevalence of hypercholesterolemia was significantly higher in the hypertension group (12.33%), compared with controls (4%). The prevalence of other variables was significantly higher in the hypertension group (12.33%), compared with controls (4%). The prevalence of other variables was significantly higher in the hypertension group: Raised LDL-C (9.7% for hypertension group and 3.3% for controls, p=0.017), triglyceride (7.33% vs 2.7%, p=0.045). The prevalence of low HDL-C and physical inactivity were higher in the hypertension group, though no statistical difference was observed in both groups. The percentage of postmenopausal women in both study groups is similar. Alcohol consumption was generally low and comparable in both groups. None of the study participants had a history of current or previous smoking. Sixty-seven (22.3%) hypertensive women had clinical and laboratory features of metabolic syndrome as compared with 9.3% of the control group, and this was statistically significant. These are as shown in Table 3 below.

CV risk factor	HTN subjects, N (%)	Control, N (%)	p value Č	
IFG/DM	25 (8.3)	7 (4.7)	0.154	
BMI ≥30 kg/m²	112 (37.7)	33 (22)	0.001	
Truncal Obesity	157 (52.3)	45 (30)	0.001	
Hypercholesterolemia	37 (12.33)	6 (4)	0.001	
Raised LDL-C	29 (9.7)	5 (3.3)	0.017	
Low HDL-C	24 (8)	8 (5.3)	0.299	
Hypertriglyceridemia	22 (7.33)	4 (2.7)	0.045	
Cigarette smoking	0	0		
Alcohol $> 3$ units/day	13 (4.3)	7 (4.7)	0.872	
Physical Inactivity	8 (2.7)	3 (2)	0.666	
Post-menopausal	197 (65.7)	95 (63.3)	0.625	
Metabolic Syndrome	67 (22.3)	14 (9.3)	0.001	

Table 3: Frequency of cardiovascular disease risk factors and metabolic syndrome.

**Key**: **HTN**= hypertension, **IFG/DM**= impaired fasting glucose/ Diabetes Mellitus, **TC**= Total cholesterol; **TG**= Triglycerides; **LDL**-**C**= Low density lipoprotein cholesterol; **HDL**-**C**= High density

lipoprotein cholesterol; N= number of persons, %= percentage.

#### 4.3 24-hour Holter Electrocardiographic (ECG) findings

Evaluation of arrhythmias using 24-hour Holter ECG showed that 176 (59.7%) of hypertensive subjects and 50 (33.3%) of the controls had arrhythmias, as shown in Table 4.

Premature ventricular complex (PVC) was the commonest type of arrhythmias in both groups. PVC was significantly more prevalent in the hypertension group (32.3%) compared to 22% in the controls followed by premature atrial contractions (PAC). One hundred and twenty-four (41.3%) hypertensive patients had normal Holter ECG findings compared to 100 (66.7%) subjects in the control group. Fourteen (4.7%) hypertensive patients had ventricular tachycardia

while none was recorded in the control group. Fifteen (5%) and 11 (3.7%) hypertensive patients had atrial fibrillation (AF) and supraventricular tachycardia while 2(1.3%) and 3 (2%) of control group had SVT and AF respectively. About 80% of the hypertensive patients with AF are HHF patients. Six hypertensive patients had severe bradycardia (HR less than 40 beats per minute). The hypertension cohort had a total of 2753 PVCs/24 hour compared with 1132 PVCs/24 hour in the control group.

The mean minimum and maximum heart rate (HR) were  $48.22\pm11.43$  and  $143.30\pm24.38$  beats/minute in the hypertensive patients and  $46.84\pm8.19$  and  $141.99\pm18.70$  beats/minute in the control group respectively. There was no statistical difference between the mean minimum and maximum heart rate of both groups. Analysis of time domain heart rate variability (HRV) using standard deviation of normal to normal interval (SDNN) average (milliseconds) was normal in both groups but significantly lower in the hypertension group compared to the controls ( $104.99\pm34.45$  vs  $122.11\pm46.28$ , P<0.001).

Rhythm	HTN (n=300)	Controls (n=15	0) p value	•
Mean Min HR (b/min)4	8.22±11.43	46.84±8.19	0.0940	
Mean Max HR (b/min)1	43.30±24.38	$141.99 \pm 18.70\ 0.0894$		
Mean SDNN 104.99±34	1.45 122.11±4	6.28 0.001		
Total PVCs/24 hr27531	132			
	N (%)	N (%)		
Normal	124 (41.3)	100 (66.7)	0.001	
PVC	97 (32.3)	33 (22.0)	0.023	
PAC	33 (11)	10 (6.7)	0.140	
NSVT	10 (3.3)	0 (0)	0.024	
Sustained VT	4 (1.4)	0 (0)	0.164	
SVT	11 (3.7)	2 (1.3)	0.155	
AF	15 (5)	3 (2)	0.126	
Severe Bradycardia	6 (2)	2 (1.3)	0.884	

**KEY: PVC**= Premature ventricular complex; **PAC**= Premature atrial complex; **NSVT**= Non-sustained ventricular tachycardia; **VT**= Ventricular tachycardia; **SVT**= Supraventricular tachycardia; **AF**= Atrial fibrillation, **Min**=minimum, **Max**= maximum, **HR**= heart rate, **b/min**= beats per minute. **SDNN**= standard deviation of normal to normal interval

#### 4.4 Resting Electrocardiographic (ECG) findings

Evaluation of arrhythmia using resting ECG showed that 77 (25.7%) hypertensive patients and 20 (13.3%) subjects in the control group had arrhythmia. Thirty-three (11%) and 10 (3.3%) hypertensive patients had PVC and PAC, while 10 (6.6%) and 4 (2.6%) subjects in the control group had PVC and PAC respectively. Other arrhythmic pattern observed during resting ECG in hypertensive subjects were sinus tachycardia 11 (3.7%), sinus bradycardia 6 (2%), atrial fibrillation 5 (1.7%), atrial flutter 1 (0.3%), multi atrial tachycardia 1 (0.3%) and junctional extrasystoles 10 (3.4%). The control group had lesser arrhythmic burden on resting ECG with sinus tachycardia in 3 (2%), sinus bradycardia 1 (0.7%), atrial fibrillation 1 (0.7%), and junctional extrasystoles 1 (0.7%). None of the control subjects had atrial flutter or multi atrial tachycardia. The variables of arrhythmia using resting ECG were more prevalent in the hypertension group, but no statistical difference was observed in both groups.

#### V. Discussion

**5.1 Participants Characteristics** Patients with hypertension often have other major risk factors for CVD<sup>23</sup>. The current study population consisted of 300 women with systemic hypertension and 150 age and sex-matched controls. The mean age of hypertensive patients was 57.15±11.58 years which is similar to the findings from another studies<sup>24-25</sup>. The anthropometric characteristics including mean weight, BMI, waist circumference and waist-hip ratio were significantly higher in hypertensive women compared to the control group. There were high prevalence rates of generalized and abdominal obesity which is comparable with findings by Sani et al<sup>26</sup> who reported generalized obesity of 29.2% and abdominal obesity of 67.3% in apparently healthy adult women in Katsina state. In the *Heart of Soweto Study*<sup>27</sup>, 44% of patients with systemic hypertension were obese. In addition, Amira et al<sup>28</sup> in a 5-year community-based screening in South-West Nigeria, reported that women had overweight and obesity rates of 31.9% and 29.5% respectively. The burden of obesity, especially in hypertensive women in both studies<sup>27,28</sup> are similar to this study. Tharkar et al<sup>29</sup> in a study on effect of obesity on cardiovascular risk factors in an urban population of South India reported increasing cardiovascular abnormalities with increasing BMI.

Adebayo et al<sup>30</sup> reported that the overall crude prevalence of overweight and obesity in 3 rural communities of Ife were 20.8% and 8.4% respectively. The lower prevalence reported by Adebayoand colleagues may be attributable to younger study population with a mean age of  $36.3\pm14.3$  years, the rural population and participation of men in the study. Adedoyin et al<sup>31</sup>, in a study of *Obesity in adult residents of Ile-Ife*, reported a crude prevalence of overweight and obesity of 22.1% and 14.5% in women. Obesity prevalence in normotensive women in the current study is comparable to the findings by Adedoyin and colleagues.

Obesity is associated with increased prevalence of cardiometabolic risk. Cardiometabolic abnormalities associated with obesity are due to insulin resistance, glucose intolerance, dyslipidaemia, systemic hypertension and a prothrombotic-inflammatory profile<sup>32</sup>. The INTERHEART global case-control study of 6787 women from 52 countries reported that abdominal obesity was more predictive of myocardial infarction than BMI alone<sup>33</sup>.

The mean blood sugar, total cholesterol, LDL cholesterol, triglyceride, urea/creatinine and atherogenic index were significantly higher in the hypertension group, as observed in several previous studies<sup>34-39</sup>.

Body fat distribution, especially visceral fat as observed to be more prevalent in hypertension group in current study is associated with obesity-related diseases such as DM, glucose intolerance, dyslipidaemia, CAD and systemic hypertension<sup>40</sup>.

The hypertension group showed significantly lower mean PCV and serum sodium than control group. Sub-analysis of the hypertension subjects revealed that HHF had significantly lower mean sodium (132.73 $\pm$ 3.87mmol/L) and PCV (37.40 $\pm$ 4.18%) as compared with hypertension patients without heart failure. Hyponatremia was present in about 20% of patients admitted to hospital for heart failure and has been shown to increase mortality in the heart failure population<sup>41-43</sup>. Hyponatremia in heart failure is due to inappropriate vasopressin activity despite hypoosmolality and volume overload as well as diuretic use.

Sixty-seven (22.3%) patients in the hypertension group had metabolic syndrome. Ogbu et al<sup>39</sup>, in a study on *metabolic syndrome in hypertensive Nigerians* reported a prevalence of 54% in hypertensive women. The higher prevalence in the study by Ogbu and colleagues may be attributable to the fact that the cut-off age of the study participants was  $\geq$  35 years. Ramos et al<sup>44</sup> reported 29% metabolic syndrome in non-Hispanic Black women of childbearing age in the *National Health and Nutrition Examination Surveys* (NHANES, 1999-2004). The higher prevalence reported in this study may be due to dietary lifestyle, physical inactivity and affluent economy of USA.

It is noteworthy that 52.3% of hypertensive women in current study had truncal obesity. Insulin resistance and increased visceral fat are the hallmarks of cardiometabolic syndrome, an assembly of risk factors for developing diabetes mellitus and cardiovascular disease. Visceral adiposity increases the degree of insulin resistance associated with obesity<sup>45</sup>.

None of the study participants was a cigarette smoker. Ogunmola et al<sup>39</sup> in a study of cardiovascular risk factors among adults in a rural community in Southwest Nigeria reported a 2.8% prevalence of current smokers in women.

## 5.2. Evaluation of arrhythmias in Hypertensive Subjects.

Cardiac arrhythmias secondary to hypertensive heart disease may be due to increase in systemic catecholamines, electrolyte derangements and associated heart failure<sup>8</sup>.

A significantly higher number (about 60 percent) of hypertensive patients in this study had arrhythmia on Holter ECG compared with 33.3% of control group. Premature ventricular complex (PVC) was the commonest type of arrhythmias in both groups but found more prevalent in the hypertension group (32.3% in hypertensive subjects and 22% in control group), followed by premature atrial contractions. Okeahialam<sup>46</sup> reported ventricular ectopy as the commonest arrhythmia in a study of 1547 resting ECG tracings over a 5-year period in Jos, Nigeria. Fourteen (4.7%) hypertension subjects had ventricular tachycardia, while 15 (5%) had AF. About 80% of the hypertensive patients with AF are HHF patients. The high prevalence of AF in HHF subgroup is worrisome. Previous studies in Nigeria have documented similar arrhythmic findings<sup>6,47-48</sup>. Familoni et al<sup>49</sup> reported that AF was associated with increased mortality rates among patients with advanced heart failure.

The HRV using SDNN average (millisecond) were significantly lower in the hypertension group. Previous studies in Nigeria have documented similar findings<sup>6,47</sup>.

#### VI. Conclusion:

This study has shown that hypertensive women had significantly highercardiovascular disease risk factors. There is a greater arrhythmic burden in hypertensive women than in the control (59.7% vs 33.3%) with premature ventricular complex being the commonest arrhythmic pattern. Early risk factor detection and treatment by assessing CVD risk factors in women with hypertension, in primary care is recommended.

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#### **References:**

- [1]. Ogah OS, Okpechi I, Chukwunonye II, Akinyemi OJ, Onwubere JCB, Falase AO, et al. Blood pressure, prevalence of hypertension and hypertension related complications in Nigerian Africans: A review. World J Cardiol. 2012; 4(12): 327-340.
- [2]. Wolf-Maier K, Cooper RS, Banegas JR, Giampoli S, Hense HW, Joffres M, et al. Hypertension prevalence and blood pressure levels in 6 European countries, Canada and the United States. JAMA. 2003; 289:2363-2369.
- [3]. Karaye KM, Okeahialam BN, Wali SS. Cardiovascular risk factors in Nigerians with systemic hypertension. Niger J Med.2007; 16(2):119-24.
- [4]. Regitz-Zagrosek V. Sex and gender differences in cardiovascular disease. In: Oertelt-PrigioneS, &Regitz-Zagrosek V, Editors. Sex and Gender Aspects in Clinical Medicine, London; Springer Verlag. 2012;12: p.17-45.
- [5]. Jean-Phillipe B, Jean-Michel M. Hypertension and Arrhythmia. EurSoc Hypertension Scientific Newsletter. 2005;6: No 24.
- [6]. Adebayo RA, Ikwu AN, Balogun MO, Akintomide AO, Mene-Afejuku TO, Adeyeye VO, et al. Evaluation of the indications and arrhythmic pattern of 24-hour Holter electrocardiography among hypertensive and diabetic patients seen at OAUTHC, Ile-Ife, Nigeria. Diabetes MetabSyndrObes. 2014;7: 565-70.
- [7]. .Simpson RJ Jr, Cascio WE, Schreiner PJ, Crow RS, Rautaharju PM, Heiss G. Prevalence of premature ventricular contractions in a population of African American and White men and women: the Atherosclerosis Risk in Communities (ARIC) study. Am Heart J. 2002; 143:535-40.
- [8]. Omotoso ABO, Opadijo OG, Araoye MA. Arrhythmias in hypertensive heart disease; a study of 2017 Nigerian patients. NigQt J Hosp Med. 1997;7(4):310-13.
- [9]. Mosca L, Mochari H, Christian A, Berra K, Tanbert K, Mills T, et al. National study of women's awareness, preventive action, and barriers to cardiovascular health. Circulation. 2006; 113:525-9.
- [10]. Lloyd-Jones DM, Larson MG, Beisser A, Levy D. Lifetime risk of developing coronary heart disease. Lancet. 1999; 353:89-92.
- [11]. Mosca M, Manson JE, Sutherland SE, Langer RD, Manolio T, Barret-Connor E. Cardiovascular disease in women. Circulation.1997; 96:2468-2482.
- [12]. Tandon VR, Mahajan A, Sharma S, Sharma A. Prevalence of cardiovascular risk factors in postmenopausal women: A rural study. J Midlife Health. 2010; 1(1): 26-29.
- [13]. Araoye MO. Research methodology with statistics for health and social sciences. Ilorin: Nathadex Publishers.2004; 1:115-120.
- [14]. Adebayo RA, Balogun MO, Adedoyin RA, Obashoro-John OA, Bisiriyu LA, Abiodun AO. Prevalence of hypertension in three rural communities of Ife North Local Government Area of Osun State, South West Nigeria. Int J Gen Med. 2013; 6: 863-868. doi: 10.2147/IJGM.S51906
- [15]. Guidelines subcommittee: 1999 WHO/ISH guidelines for the management of hypertension. J Hypertens. 1999; 17: 151-183.
- [16]. NHS Lothian Health Promotion Service: Current daily sensible drinking guidelines for adults. Available at: http://www.nhslothian.scot.nhs.uk.
- [17]. World Health Organization: Prevention and managing the global epidemic of obesity. Report of the World Health Organization consultation on obesity WHO, Geneva 1997.
- [18]. Nkado RN, Onwubere BJC, Ikeh VO, Anisiuba BC. Correlation of electrocardiogram with echocardiographic left ventricular mass in adult Nigerians with systemic hypertension. West Afr J Med. 2003; 22(3): 246-249.
- [19]. Kligfield P, Gettes L, Bailey JJ. Recommendation for the standardization and interpretation of the electrocardiogram: Part 1: The electrocardiogram and its technology: A scientific statement from the American Heart Association Electrocardiography and Arrhythmias Committee, Council on Clinical Cardiology, the American College of Cardiology Foundation, and the Heart Rhythm Society: endorsed by the International Society for Computerized Electrocardiology. Circulation.2007; 115:1325-1332.
- [20]. MT-101/MT-200 [package insert]. Baar, Switzerland: Schiller; 2004.
- [21]. American Diabetic Association: Diagnosis and classification of diabetes mellitus. Diabetes care. 2010; 33(1): 562.
- [22]. Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults: National Cholesterol Education Programme: Report of the Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol (Adult Treatment Panel III). JAMA. 2001, 29: 395-409.
- [23]. Weycker D, Nichols GA, O'Keeffe-Rosetti M, Edelsberg J, Khan ZM, Kaura S, et al. Risk-factor clustering and cardiovascular disease risk in hypertensive patients. Am J Hypertens. 2007 Jun;20(6): 599-607.
- [24]. Akintunde AA, Akinwusi PO, Adebayo RA, Ogunyemi S, Opadijo OG. Burden of obesity in essential hypertension. Nig J Clin Pract.2010; 13(4):399-402.
- [25]. Aje A, Adebiyi AA, Oladapo OO, Dada A, Ogah OS, Ojji DB, et al. Left ventricular geometric patterns in newly presenting Nigerian hypertensives: An echocardiographic study. BMC Cardiovascular Disorders. 2006; 6:4. <u>http://www.biomedcentral.com/1471-2261/6/4</u>.
- [26]. Sani MU, Wahab KW, Yusuf BO, Gbadamosi A. Modifiable cardiovascular risk factors among apparently healthy adult Nigerian population- a cross sectional study. Biomed Central Res Notes. 2010;3: 11.doi.10.1186/1756-0500-3-11.
- [27]. 27. Ruf V, Stewart S, Pretorius S, Khubheka M, Lautensschlager C, Presek P, et al. Medication adherence, self-care behavior and knowledge of heart failure in urban South Africa: the Heart of Soweto Study. Cardiovasc J Afr. 2010;21(2): 86-92.
- [28]. Amira CO, Sokunbi DOB, Dolapo D, Sokunbi A. Prevalence of obesity, overweight and proteinuria in an urban community in South West Nigeria. Nig Med J.2011; 52(2): 110-113.

- [29]. Thakar S, Viswanathan V. Effect of obesity on cardiovascular risk factors in urban population in South India. Heart Asia. 2010: 145-149. Doi:10.1136/ha.2009.000950.
- [30]. Adebayo RA, Balogun MO, Adedoyin RA, Obashoro-John OA, Bisiriyu LA, Abiodun OO. Prevalence and pattern of overweight and obesity in three rural communities in Southwest Nigeria. Diabetes MetabSyndrObes. 2014; 7: 153-158.
- [31]. Adedoyin RA, Mbada CE, Balogun MO, Adebayo RA, Martins T, Ismail S. Obesity prevalence in adult residents of Ile-Ife, Nigeria. Nig Q J Hosp Med. 2009; 19 (1): 63-68.
- [32]. Conier M, Despres J, Davis N, Grossniklaus DA, Klein S, Lamarche B, et al. Assessing Adiposity: A Scientific Statement from the American Heart Association. Circulation. 2011;124: 1996-2019.
- [33]. Anand SS, Islam S, Rosengren A. Risk factors of myocardial infarction in women and men: Insights from the INTERHEART study. Eur Heart J.2008; 29:932-40.
- [34]. Ogbu ISI, Neboh CI. The prevalence of prediabetes among hypertensive patients in Enugu, Southeast Nigeria. Niger Med J. 2009; 50: 14-17.
- [35]. Wei W, Li Y, Chen F, Chen C, Sun T, Sun Z, et al. Dyslipidaemia, combined oral contraceptives use and their interaction on the risk of hypertension in Chinese women. Journal of Human Hypertension. 2011; 25: 364-371.
- [36]. Coresh J, Wei GL, McQuillan G, Brancati FL, Levey AS, Jones C, et al. Prevalence of high blood pressure and elevated serum creatinine level in the United States: findings from the third National Health and Nutrition Examination Survey (1988-1994). Arch Intern Med. 2001 May 14;161 (9): 1207-16.
- [37]. Nwagha UI, Ikekpeazu EJ, Ejezie FE, Neboh EE, Maduka IC. Atherogenic index of plasma as a useful predictor of cardiovascular risk among postmenopausal women in Enugu, Nigeria. African Health Sciences. 2010; 10(3): 248-252.
- [38]. Ogbu ISI, Ugwuja EI. Metabolic syndrome in Hypertensive Nigerians: Risk factor analysis. IOSR Journal of Pharmacy and Biological Sciences (IOR-JPBS).2012;4(1): 28-32. <u>www.iosrjournals.org</u>.
- [39]. Ogunmola OJ, Olaifa AO, Oladapo OO, Babatunde OA. Prevalence of cardiovascular risk factors among adults without obvious cardiovascular disease in a rural community in Ekiti State, Southwest Nigeria. BMC Cardiovascular Disorders.2013;13: 89.doi:10.1186/1471-2261-13-89. http://www.biomedcentral.com/1471-2261/13/89.
- [40]. Klein S, Allison DB, Heymsfield SB, Kelley DE, Liebel RL, Nonas C, et al. Waist circumference and cardiometabolic risk: A consensus statement from Shaping America's Health; Association for Weight Management and Obesity Prevention; NASO, The Obesity Society; The American Society for Nutrition; and the American Diabetes Association. Am J Clin Nutr.2007;85:1197-202.
- [41]. Sica DA. Sodium and water retention in heart failure and diuretic therapy: basic mechanisms. Cleveland Clinic Journal of Medicine. 2006; 73(2):30-33.
- [42]. Goldberg A, Hammerman H, Petcherski S, Nassar M, Zdorovyak A, Yalonetsky S, et al. Hyponatremia and long-term mortality in survivors of acute ST-elevation myocardial infarction. Archives of Internal Medicine. 2006; 166(7): 781-786.
- [43]. De Luca L, Klein L, Udelson JE, Orlandi C, Sardella G, Fedele F, et al. Hyponatremia in patients with heart failure. Am J Cardiol. 2005; 96(12): 19-23.
- [44]. Ramos RG, Olden K. The prevalence of metabolic syndrome among US women of childbearing age. Am J Public Health. 2008; 98(6): 1122-1127.
- [45]. Bray GA. Risk of obesity. EndocrinolMetabClin N Am. 2003; 32:787-804.
- [46]. Okeahialam BN. The burden of arrhythmia in hypertension: an electrocardiographic study. Nig J Cardiol. 2004; 1:53-56.
- [47]. Adebayo RA, Ikwu AN, Balogun MO, Akintomide AO, Ajayi OE, Adeyeye VO, et al. Heart rate variability and arrhythmic patterns of 24-hour Holter electrocardiography among Nigerians with cardiovascular diseases. Vascular Health and Risk Management. 2015; 11:1-7.
- [48]. Katibi IA, Beshir S, Mudashiru Z. Ambulatory 24-hour Holter electrocardiography among Nigerians: Our experience at a referral cardiac center in Lagos, Nigeria. Niger Med J.2006; 47(2): 25-27.

DrAmanzeIkwu, et. al. "Cardiovascular Disease Risk Factors and Arrhythmia Burden in Hypertensive Women: A Cross-sectional Study in a Semi-urban African Community." *IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)*, 19(8), 2020, pp. 54-63.

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