

Association between blood pressure dipping patterns and hypertension-mediated organ damage among Nigerians with newly-diagnosed hypertension

*Dele-Ojo, B.F.¹, Ogunmodede J.A.², Ojo O.D.³, Kolo P.M.², Katibi I.A.², Omotoso A.B.², Adeoye M.A.⁴, Adesokan A.⁵

Abstract

Introduction: Abnormal blood pressure (BP) dipping patterns are associated with increased cardiovascular risk among Africans. This study determined the association between BP dipping patterns and hypertension-mediated organ damage among patients with newly-diagnosed hypertension.

Methods: Ambulatory BP monitoring and echocardiography were carried out on 120 participants. Participants were categorized based on the ratio of night-time to day-time systolic BP into 4 patterns: Normal dipper (10% but < 20%), non-dippers (0% but < 10%), reverse dippers (<0%) and extreme dippers (> 20%).

Result: Fifty-one (42.5%) were males, the mean age and body mass index were 44.2±9.8years and 27.1±4.4kg/m² respectively. The non-dipping pattern was the most prevalent while the reverse dipping had the lowest mitral E/A ratio. Office systolic blood pressure was the only predictor of left ventricular hypertrophy (OR=1.050, 95% CI=1.004-1.098; p-value = 0.034).

Conclusions: The non-dipping pattern was the most prevalent abnormal dipping pattern while the reverse dippers had the highest risk of hypertension-mediated organ damage. Office blood pressure was the only predictor of left ventricular hypertrophy. Hence, office BP measurement as well as ambulatory blood pressure measurements are potentially important tools in risk stratification in resource-poor settings of sub-Saharan Africa.

Keywords: Dipping patterns, hypertension-mediated organ damage, echocardiography, left ventricular hypertrophy, Nigeria.

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Association entre les schémas de baisse de la pression artérielle et les lésions organiques induites par l'hypertension chez les Nigériens souffrant d'hypertension nouvellement diagnostiquée

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Resume

Introduction: Les baisses de tension artérielle (TA) anormales sont associées à un risque cardiovasculaire accru chez les Africains. Cette étude a déterminé l'association entre les schémas de baisse de la PA et les lésions organiques induites par l'hypertension chez les patients souffrant d'hypertension nouvellement diagnostiquée.

Méthodes: Une surveillance ambulatoire de la PA et une échocardiographie ont été réalisées sur 120 participants. Les participants ont été classés en fonction du rapport de la PA systolique nocturne à la PA systolique diurne en 4 modèles : balancier normal (=10 % mais < 20 %), non-dippers (=0 % mais < 10 %), balanciers inversés (< 0 %) et les plongeurs extrêmes (=20 %).

Résultat : Cinquante et un (42,5 %) étaient des hommes, l'âge moyen et l'indice de masse corporelle étaient respectivement de $44,2 \pm 9,8$ ans et de $27,1 \pm 4,4$ kg/m². Le modèle sans pendage était le plus répandu tandis que le pendage inversé avait le rapport E/A mitral le plus faible. La pression artérielle systolique en cabinet était le seul prédicteur de l'hypertrophie ventriculaire gauche (OR = 1,050, IC à 95 % = 1,004-1,098 ; valeur p = 0,034).

Conclusions: Le modèle sans pendage était le modèle anormal de trempage le plus répandu, tandis que les plongeurs inversés présentaient le risque le plus élevé de dommages aux organes liés à l'hypertension. La pression artérielle en cabinet était le seul facteur prédictif d'hypertrophie ventriculaire gauche. Par conséquent, la mesure de la PA en cabinet ainsi que les mesures ambulatoires de la pression artérielle sont des outils potentiellement importants dans la stratification du risque dans les milieux à faibles ressources de l'Afrique subsaharienne.

Mots-clés: schémas de trempage, lésions organiques induites par l'hypertension, échocardiographie, hypertrophie ventriculaire gauche, Nigéria.

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INTRODUCTION

Systemic hypertension (SH) is a global public health problem and a leading cause of death worldwide (1). Hypertension is more common among African population groups and they have a higher incidence of hypertension-related cardiovascular disease when compared with people of other races (2-4). However, the optimal management of SH begins with appropriate diagnosis and proper classification of blood pressure (BP) phenotypes. Identifying the BP dipping patterns will help in further risk stratification of patients with newly-diagnosed hypertension. Twenty-four (24)-hour ambulatory blood pressure monitoring (ABPM) has been encouraged by the European Society of Cardiology guideline in patients with newly-diagnosed SH (5). The evaluation of BP circadian profiles and the diagnosis of nocturnal hypertension are some of the benefits of ABPM (5). Ambulatory night-time BP value is a better predictor of cardiovascular disease (CVD) risk when compared with the daytime BP value (6). The night-time ABPM value provides additional predictive information over daytime ABPM value (7). The night-time systolic BP is the most potent predictor of cardiovascular event and mortality (7,8). Higher night-time systolic BP was found to be associated with all-cause mortality, while both higher night-time systolic BP and diastolic BP were associated with increased risk of cardiovascular disease (coronary heart disease and stroke) (9,10). A previous study revealed that night-time dosing with antihypertensive medications reduced major cardiovascular events such as CVD death, stroke and myocardial infarction by 67%, probably because of night-time BP attenuation effect (6).

Some local studies done, were mostly on the prevalence of circadian rhythm in patients with hypertension (11-13), but there is a dearth of studies on the association between blood pressure dipping patterns and *hypertension-mediated organ damage* among patients with hypertension. Hence, this study determined the association between BP dipping patterns and *hypertension-mediated organ damage* among Nigerian patients with newly-diagnosed hypertension.

MATERIALS AND METHODS

A cross-sectional study that consisted of 120 patients with newly-diagnosed SH, who were 18 years and above. All participants gave written informed consent. Participants were seen at the Medical Outpatient Departments of UITH between June 2014 to December 2014. The

patients in this study were antihypertensive-naïve adults whose systolic blood pressure (SBP) were equal to or greater than 140mmHg and /or diastolic blood pressure (DBP) of equal to or greater than 90mmHg (14). Individuals with other co-morbidities and pregnant females were excluded from the study. ABPM and echocardiography were carried out on all the study participants. They were recruited consecutively. Each patient had the office BP measured by the auscultatory method in both arms using the mercury sphygmomanometer while relaxed and sitting down with both feet resting on the floor. The mean of three BP readings in the arm with the higher BP reading was taken as the patients' office BP. Both the systolic and diastolic BP were determined to the nearest 2 mmHg. This was followed by 24-hour ABPM using CONTEC ambulatory blood pressure monitors according to the recommendations of the European Society of Hypertension practise guidelines (15). The procedure and handling of the ambulatory blood pressure monitor were explained to the subjects after which patients' details were entered and the monitoring was initialized. The machine was programmed to read half-hourly from 7 a.m. to 10 p.m. and hourly from 10 p.m. to 7 a.m, in order to reduce the frequency of interference with sleep during the night-period. An appropriate cuff size was chosen and this was applied immediately to the participant's non-dominant bare arm. Participants were discharged home to continue their normal activities and were asked to return after 24 hours for retrieval of the ABP monitor. They were advised to avoid any activity during the measurements and to abstain from smoking, alcohol use and the consumption of caffeinated drinks throughout the period of study.

Dipping pattern was categorized as follows (15): Normal dipping pattern occurred when the reduction in the mean SBP during the night period was greater than or equal 10% but lesser than 20% of mean SBP during the day (that is: 10% but <20%); non-dipping pattern occurred when the reduction in the mean SBP during the night was greater than or equal to 0% but lesser than 10% of mean SBP during the day (that is 0% but < 10%); reverse dipping pattern occurred when mean night-time BP was greater than the mean of day-time BP and the nocturnal dip was less than 0%; extreme dipping pattern (extreme dippers) occurred when night-time SBP fall was greater than or equal to 20% (that is 20%) of the mean day-time SBP.

Echocardiography

Two-dimensional transthoracic echocardiography was carried out by a Cardiologist with training in echocardiography using Sonos-2,000; Philips Medical Systems, Amsterdam, Netherlands and standardized protocols. (16) Left ventricular dimensions including left ventricular internal diameter in diastole (LVIDd), interventricular septal thickness in diastole (IVSd), and posterior wall thickness in diastole (PWTd), were assessed according to American Society of Echocardiography (ASE) recommendations (16).

Left ventricular mass index (LVMI) was calculated using the ASE – cubed formula (16):

$$\text{LVMI(g/m)} = \frac{1.04[(\text{LVIDD} + \text{PWTd} + \text{IVSd})^3 - (\text{LVIDD})^3] - 0.8 + 0.6}{\text{BSA}}$$

Where BSA is Body Surface Area.

Left ventricular hypertrophy (LVH) was defined as increased LVMI 96 g/m^2 in women and 116 g/m^2 in men (17,18).

Additionally, doppler echocardiography was obtained according to the recommendations of quantification of Doppler Echo of the ASE (16). The LV diastolic flow pattern was assessed by Doppler studies via the Apical 4-chamber and 5-chamber views. The trans-mitral, pulmonary and aortic velocities were determined. The mitral inflow E and A velocities were recorded as the mitral E/A ratio. The deceleration time (DT) and isovolumetric relaxation time (IVRT) were also obtained. Pulmonary venous flow (PVF) velocity recording was carried out via the apical 4 chamber view using the pulsed wave Doppler by placing the cursor in the right upper pulmonary vein close to the inter-atrial septum. By this, the peak systolic S and diastolic D flow velocities and the ratio of S/D, AR (atrial reversal) were obtained. Peak early transmitral filling velocity (E), peak late trans-mitral filling velocity (A), the ratio of early and late trans-mitral filling velocity (E/A), deceleration time (DT) of the early transmitral filling velocity, isovolumetric relaxation time (IVRT) is the time interval between aortic valve closure and mitral valve opening.

The LV diastolic function was classified as (16):

Normal: E/A ratio = 1 – 2, DT = 160 – 240msecs.

Impaired relaxation: Reduced E velocity, increased A velocity; E/A ratio < 1, prolonged DT (>200msec), prolonged IVRT (>100msec), S>D

Pseudonormalization: E/A ratio = 1 - 2;

DT = 160 - 240msecs, S<D.

Restrictive Pattern: E/A ratio >2 (that is increased E velocity, decreased A velocity), shortened DT (<160ms) shortened IVRT (<60msec).

Ethical approval was obtained from the ethics and research committee of UIITH with approval protocol number ERC/2015/06/07.

Statistical Analysis

The data were analysed using the Statistical Package for Social Sciences (SPSS) version 23. Categorical variables were expressed as proportions and percentages while continuous variables were expressed as means with standard deviations (SD). Participants' characteristics were calculated for the overall sample and later stratified into three dipping patterns (normal dipping, non-dipping, and reverse dipping). Using analysis of variance (ANOVA), the mean of the 3 categories of blood pressure dipping patterns groups was compared and post-hoc analysis was done with the Tukey test for multiple pair-wise comparisons to determine where the significance lies. Binary logistic regression was used to determine the predictors of LVH. For all tests, a p-value < 0.05 was taken as being statistically significant.

RESULTS

The general characteristics of the study population, including office BP, ambulatory blood pressure and the echocardiographic indices are shown in Table 1. A total of 120 participants completed the study, which included 51 (42.5%) male and 69 (57.5%) female patients. The mean age was 44.2 ± 9.8 years and mean body mass index (BMI) of $27.1 \pm 4.4 \text{ kg/m}^2$.

Three blood pressure dipping patterns were reported as no participant exhibited extreme BP dipping pattern. Dipping, non-dipping, and reverse dipping were reported in 21 (21.7%), 61 (50.8%), and 33 (27.5%) participants respectively, as shown in figure 1. The non-dipping pattern was the most prevalent of the circadian rhythm abnormalities. Clinical characteristics of the three BP dipping patterns is shown table 2. Participants with the reverse BP dipping pattern were older than the dippers and the non-dippers (48.8 ± 8.6 years vs 43.1 ± 9.6 vs 42.1 ± 9.8 years) respectively; p-value = 0.005. The mean 24-hour SBP, daytime SBP, and night-time SBP and DBP differ significantly. Patients with the reverse BP dipping pattern had the lowest mitral E/A ratio compared with the normal dipping and non-dipping patterns (1.0 ± 0.3 vs 1.3 ± 0.5 vs 1.1 ± 0.3) respectively; p-value = 0.006.

The characteristics of those with LVH and without LVH are shown in table 3. Office SBP is the only predictor of LVH in the study population (Odds ratio=1.05, 95% confidence interval =1.00-1.10, 0.034). Every unit increase in office SBP increased the chance of developing LVH by 5%.

DISCUSSION

In this study, the non-dipping pattern was the most prevalent abnormality of diurnal BP variation in our patients with newly diagnosed hypertension, which is similar to previous studies (11,19). We have shown that patients with the reverse dipping pattern had the lowest mitral E/A ratio, hence they were at greatest risk of diastolic dysfunction and hypertension-mediated organ damage. Additionally, this study showed office blood pressure was the only predictor of left ventricular hypertrophy. Other previous studies have also linked the non-dipping BP pattern with target organ damage and a higher risk of cardiac and extracardiac morbidity and mortality (10,20); while associating this diurnal BP variation with factors such as advanced age, stress, poor social support, low socioeconomic status, sleep quality and quantity, apnoea, anger/temperament and personality types (10,20).

Similar to previous studies, the reverse dippers were older and had higher mean 24-hour SBP, day-time SBP & DBP, mean night-time SBP & DBP than the normal dippers and the non-dippers respectively. These findings are in concordance with a previous study that showed that reduced dipping patterns were commoner in the older age groups than in the younger age-groups (21). An association between higher 24-hour ABPM measurement and increased cardiovascular mortality, myocardial infarction and stroke has been documented (22). Some other researchers have also described a linear and inverse relationship between cardiovascular mortality and the nocturnal decline in BP with every 5% decline in nocturnal dip, being associated with 20% rise in the risk of cardiovascular death (22). Furthermore, reverse dipping pattern has been previously associated with obstructive sleep apnoea, which also portends an increased cardiovascular risk (23). In particular, reverse dippers with essential hypertension have been found to have more advanced hypertension-mediated organ damage (24-29). Therefore, patients with hypertension who have the reverse dipping pattern are at the highest risk of target organ damage and consequent complications. Furthermore, a higher

night-time (nocturnal) BP measurement was reported to be significantly associated with greater risks of death and composite cardiovascular outcomes (non-fatal coronary event, heart failure and stroke) in a large population-based cohort study involving adults in Europe, Asia and South America (22). Underlying pathophysiologic mechanisms that have been suggested include factors such as abnormal neurohormonal regulation, lack of exercise, consumption of excess dietary sodium, and tobacco smoking have been implicated in the decline in nocturnal BP (30).

Finally, the study revealed that those with LVH had higher office SBP and DBP, 24-hour SBP & DBP, daytime SBP & DBP, and only night-time DBP values. We however found office SBP to be the only independent predictor of left ventricular hypertrophy in our study population. However, a number of the studies have shown that ambulatory BP measurements were better predictors of *hypertension-mediated organ damage* than office BP (6,7,31). Noteworthy, Odili *et al.* showed that office BP measurement may still have a significant role in risk stratification in resource-poor settings of sub-Saharan Africa (32).

CONCLUSION

This study revealed that the non-dipping pattern was the most prevalent abnormality of diurnal BP variation. Secondly, the reverse dippers had the lowest mitral E/A ratio putting them at the greatest risk of diastolic dysfunction. Lastly, office blood pressure was the only predictor of left ventricular hypertrophy. Hence, office BP measurement as well as ambulatory blood pressure measurements are important tools in risk stratification in resource-poor settings of sub-Saharan Africa.

Study Strengths: There is dearth of data on 24-hour ABPM in hypertensive patients in Nigeria and sub-Saharan Africa. This study is one of the first studies in the country, on the association between blood pressure dipping patterns and hypertension-mediated organ damage among patients with hypertension. This study will add to the few published data in this field.

Also, the data used in the research was collected first-hand by the researchers having carefully and rigorously designed the method to ensure accuracy, quality, and integrity. The data for the main study was collected data from real sample populations. Furthermore, the researchers did not experience any event suggesting that the

people may have given unacceptable or untruthful data because the readings were electronically measured from the BP machine.

Limitation of the study: The data are cross-sectional, hence casual inference is weak. However, hypotheses generated from it can be further tested in other centres in the country.

Authors' contributions: DBF, OJA, OOD, KPM, KIA, OAB, AMA, AA were involved in the conception and design of the study data collection, collation, data analysis, data interpretation, and manuscript proofreading.

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Table 1: General Characteristics of the Study Population

Variable	N=120 Mean ± SD
Gender	
Male, n (%)	51 (42.5%)
Female, n (%)	69 (57.5%)
Age (years)	44.2 ± 9.8
Body Mass Index (Kg/m ²)	27.1 ± 4.4
Waist Circumference (cm)	90.1 ± 13.1
Waist-hip Ratio	0.9 ± 0.1
Systolic Blood Pressure (mmHg)	152.9 ± 17.2
Diastolic Blood Pressure (mmHg)	95.8 ± 12.4
Average Total Systolic BP (mmHg)	136.8 ± 14.3
Average Total Diastolic BP (mmHg)	83.7 ± 11.4
Daytime Systolic Blood Pressure (mmHg)	137.9 ± 14.2
Daytime Diastolic Blood Pressure (mmHg)	85.1 ± 11.6
Night-time Systolic Blood Pressure (mmHg)	132.1 ± 17.2
Night-time Diastolic Blood Pressure (mmHg)	78.7 ± 11.6
Left atrial diameter (cm)	3.5 ± 0.5
Left ventricular end-diastolic diameter (cm)	4.6 ± 0.5
Left ventricular end-systolic diameter (cm)	3.0 ± 0.5
Left ventricular mass (g)	139.7 ± 36.4
Relative wall thickness	0.5 ± 0.0
Ejection fraction (%)	64.8 ± 7.9
Fractional shortening (%)	35.8 ± 6.2
Mitral E/A ratio	1.1 ± 0.3
Deceleration time (ms)	179.1 ± 74.9
Isovolumetric time(ms)	107.8 ± 16.8

Key: SD, standard deviation

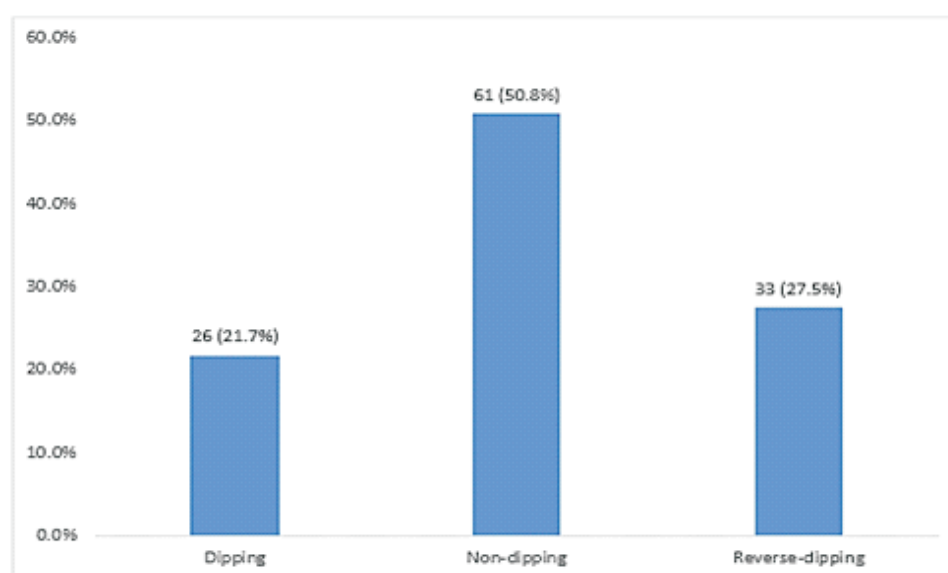
**Figure 1: Prevalence of blood pressure dipping patterns in the study population**

Table 2: Characteristics Stratified by Blood Pressure Dipping Patterns

Variable	Dippers	Non-Dippers	Reverse	p-value
	(n = 26) Mean ± SD	(n=61) Mean ± SD	Dippers (n=33) Mean ± SD	
Gender				0.201
Male, n (%)	15 (29.4)	24 (47.1)	12 (23.5)	
Female, n (%)	11 (15.9)	37 (53.6)	21 (30.4)	
LVH				0.692
Yes, n (%)	22 (84.6)	48 (78.7)	28 (84.8)	
No, n (%)	4 (15.4)	13 (21.3)	5 (15.2)	
Age (years)	43.1 ± 9.6	42.1 ± 9.8	48.8 ± 8.6	0.005* ^α
Body Mass Index (Kg/m ²)	27.0 ± 3.9	27.1 ± 3.8	27.2 ± 5.6	0.982
Waist Circumference (cm)	86.3 ± 12.2	90.5 ± 13.5	92.4 ± 12.8	0.195
Waist-hip Ratio	0.9 ± 0.0	0.9 ± 0.1	0.9 ± 0.1	0.229
Systolic Blood Pressure (mmHg)	152 ± 17.2	150 ± 14.3	159 ± 20.8	0.051
Diastolic Blood Pressure (mmHg)	97.0 ± 13.0	96.4 ± 12.0	93.8 ± 12.7	0.546
24-hour Systolic BP (mmHg)	138.3 ± 18.2	133.1 ± 11.4	142.4 ± 14.0	0.008* ^π
24-hour Diastolic BP (mmHg)	84.4 ± 12.7	82.5 ± 11.1	85.3 ± 11.1	0.496
Daytime Systolic Blood Pressure (mmHg)	142 ± 18.5	134.7 ± 11.8	140.7 ± 13.3	0.038* ^δ
Daytime Diastolic Blood Pressure (mmHg)	87.4 ± 13.1	84.1 ± 11.1	85.3 ± 11.5	0.493
Night-time Systolic Blood Pressure (mmHg)	123.3 ± 16.0	126.8 ± 10.2	148.8 ± 17.2	<0.001* ^μ
Night-time Diastolic Blood Pressure (mmHg)	72.0 ± 9.8	78.0 ± 10.8	85.1 ± 11.1	<0.001* ^β
Left atrial diameter (cm)	3.4 ± 0.7	3.6 ± 0.5	3.5 ± 0.5	0.532
LVEDD (cm)	4.6 ± 0.5	4.6 ± 0.5	4.7 ± 0.6	0.680
LVESD (cm)	2.9 ± 0.4	3.0 ± 0.5	3.0 ± 0.5	0.650
LVM (g)	254.6 ± 57.8	248.4 ± 62.5	270.5 ± 95.8	0.368
LVMI (g/m ²)	138.1 ± 32.1	134.3 ± 31.4	150.9 ± 45.6	0.105
Relative wall thickness	0.4 ± 0.0	0.5 ± 0.0	0.5 ± 0.0	0.749
Ejection fraction (%)	67.3 ± 7.7	63.9 ± 8.0	64.6 ± 7.8	0.180
Fractional shortening (%)	37.7 ± 6.3	35.1 ± 6.1	35.6 ± 6.0	0.192
Mitral E/A ratio	1.3 ± 0.5	1.1 ± 0.3	1.0 ± 0.3	0.006* ^δ
DT (ms)	186.2 ± 76.9	178.8 ± 69.1	174.1 ± 85.1	0.829
IVRT (ms)	107.8 ± 16.9	105.6 ± 17.9	111.8 ± 14.4	0.237

Keys: *, statistically significant; LA, left atrium; LVIDD, left ventricular internal dimension in diastole; LVISD, left ventricular internal dimension in systole; FS, fractional shortening; EF, ejection fraction; LVM, left ventricular mass; LVMI, left ventricular mass index; RWT, relative wall thickness; DT - deceleration time; IVRT, isovolumetric relaxation time.

Where the significance lies: α – reverse dippers significantly greater than normal dippers,

π – reverse dippers significantly greater than non-dippers, δ - normal dippers significantly greater than non-dippers, μ - reverse dippers significantly greater than normal dipping patterns.

β – reverse dipping pattern is greater than the non-dipping pattern, the non-dipping pattern is greater than the dipping pattern.

Table 3: Characteristics stratified by the presence of Left Ventricular Hypertrophy

Variables	LVH	NO LVH	p-value
	(n=98) Mean ± SD	(n=22) Mean ± SD	
Age	43.9 ± 9.8	45.5 ± 10.2	0.495
Body mass index	27.5 ± 4.4	25.6 ± 4.0	0.066
Waist circumference	91.0 ± 13.4	86.1 ± 11.3	0.111
Waist-hip ratio	0.9 ± 0.1	0.9 ± 0.1	0.673
Office Systolic Blood Pressure	154.9 ± 17.4	144.2 ± 13.3	0.008*
Office Diastolic Blood Pressure	97.1 ± 12.1	90.1 ± 12.3	0.016*
Ambulatory 24-hour SBP (mmHg)	138.2 ± 14.6	130.4 ± 10.9	0.020*
Ambulatory 24-hour DBP (mmHg)	84.8 ± 11.7	78.4 ± 8.4	0.015*
Ambulatory daytime SBP (mmHg)	139.4 ± 14.5	131.6 ± 10.6	0.019*
Ambulatory daytime DBP (mmHg)	86.4 ± 11.9	79.5 ± 8.6	0.011*
Ambulatory night-time SBP (mmHg)	133.5 ± 17.6	126.0 ± 13.7	0.065
Ambulatory night-time DBP (mmHg)	79.7 ± 11.9	74.0 ± 8.8	0.034*

Keys: SBP, systolic blood pressure; DBP, diastolic blood pressure; LVH, left ventricular hypertrophy, *, statistically significant.

Table 4: Predictor of left Ventricular hypertrophy in the Study Population

Variables	Odd Ratio	95% Confidence Interval	p-value
Age (years)	0.946	0.893 - 1.003	0.063
Waist circumference (cm)	1.035	0.994 - 1.078	0.093
Office SBP (mmHg)	1.050	1.004 - 1.098	0.034*
Office DBP (mmHg)	1.006	0.950 - 1.065	0.838
Ambulatory day-time SBP (mmHg)	0.973	0.882 - 1.075	0.593
Ambulatory day-time DBP (mmHg)	1.068	0.961 - 1.188	0.224
Ambulatory night-time SBP (mmHg)	1.008	0.943 - 1.077	0.817
Ambulatory night-time DBP (mmHg)	0.994	0.908 - 1.088	0.889

Ref – Reference category. SBP = Systolic blood pressure,

DBP = Diastolic blood pressure,

* = statistically significant.