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Research Article

Association between White Coat Hypertension and Left Ventricular Hypertrophy among Adult Nigerians.

***Dele-Ojo B.F.¹, Ogunmodede J.A², Ojo O.D³, Bello H.S², Kolo P.M², Katibi I.A², Omotoso A.B² and Dada S.A.¹**

¹*Department of Medicine, Ekiti State University Teaching Hospital, Ado-Ekiti, Ekiti state, Nigeria.*

²*Department of Medicine, University of Ilorin, PMB 1515, Ilorin, Kwara state, Nigeria.*

³*Department of Orthopaedics Surgery, Afe Babaolola University, Ado-Ekiti, Ekiti state, Nigeria.*

ABSTRACT

There has been an age-long controversy on whether white coat hypertension (WCH) is associated with end organ damage or not. Hence, the presence of left ventricular hypertrophy was assessed in individuals with WCH. This study determined the association between WCH and left ventricular hypertrophy among adult Nigerians. A total of 88 participants consisting of 44 patients with WCH and 44 age and sex-matched normotensive controls were studied. They all underwent 24-hour ambulatory blood pressure measurement and echocardiography. Thirty-one (70.5%) females were in each group. The mean body mass index of patients ($26.4 \pm 4.5\text{kg/m}^2$) was significantly higher than that of the controls ($23.8 \pm 4.3\text{kg/m}^2$). Twenty-four of 44 patients and 19 of 44 controls had left ventricular hypertrophy; (chi square=1.137, p-value=0.286). There is high but similar prevalence of LVH among participants with WCH and normotension among adult Nigerians. Hence, there is need to assess every patient with WCH for the presence of LVH and to be followed up for the development of other cardiovascular risk factors.

Keywords: *White Coat Hypertension, Left Ventricular Hypertrophy, Ambulatory Blood Pressure Measurement, Echocardiography, Nigerians.*

*Author for correspondence: bolade.dele-ojo@eksu.edu.ng; Tel: +2348033654525

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INTRODUCTION

There has been age-long controversy on whether white coat hypertension (WCH) is associated with target organ damage or not. Recent studies revealed the presence of increased end organ damage in individuals with WCH whereas older studies showed no evidence of target organ damage. (Staessen *et al.*, 1999, Pierdomenico *et al.*, 1995, Parati *et al.*, 2000b, Cuspidi *et al.*, 2018). Although cardiovascular (CV) events and target organ damage are not as common in white-coat hypertension (WCH) compared with sustained hypertension, it is yet to be fully explained whether WCH is associated with an increased CV risk and target organ damage compared with normotension among the Nigerian population. It has however been documented that WCH is associated with subclinical organ damage as indicated by elevated left ventricular (LV) mass index (LVMI). (Androulakis *et al.*, 2017, Anstey *et al.*, 2018). However, appropriate management of systemic hypertension (SH) begins with early diagnosis and

identification of individuals at risk by detection of early makers of the disease. Ambulatory blood pressure monitoring (ABPM) is considered the best method to detect blood pressure (BP) fluctuations and the most reliable method of diagnosing white coat hypertension (WCH). (Pickering, 1998). Recent researches have concluded that ABPM is a better predictor of cardiovascular (CV) mortality than office-measured pressure. (Banegas *et al.*, 2018, Huang *et al.*, 2017). ABPM can monitor BP for a 24-hour period while providing more detailed BP measurements including the day-time and night-time BP.

Left ventricular hypertrophy (LVH) is an early maker of hypertensive cardiovascular disease. (Giles *et al.*, 2005). Hence, the presence of LVH in any patient is a strong and independent risk factor for subsequent cardiovascular event. (Ferdinand and Maraboto, 2019, Cipriano *et al.*, 2001). Nevertheless, LVH is a common and potentially modifiable cardiovascular risk factor that may be associated with an

absence of symptoms for many years before the development of cardiovascular events. (Lorell and Carabello, 2000). In contemporary clinical practice and population studies, the diagnosis of LVH depends predominantly on echocardiographic measurements.

A recent study in Nigeria showed high prevalence of WCH in the study population. (Dele-Ojo *et al.*, 2019). Also, some studies have been done in Nigeria on the association between end organ damage and systemic hypertension (Nelissen *et al.*, 2014, Saidu *et al.*, 2018). However, to the best of our knowledge, none has been done to determine the association between WCH and LVH. In Nigeria, there is currently no study linking WCH and left ventricular hypertrophy. Hence, this study determined the association between WCH and LVH among adult Nigerians.

MATERIALS AND METHODS

Study design and area: This research was a cross-sectional survey conducted in the Medical Outpatient Department (MOPD) of the University of Ilorin Teaching Hospital (UITH), Ilorin, Kwara State in North-central Nigeria.

Inclusion and Exclusion criteria: Patients were adults with WCH diagnosed using ABPM while controls were normotensive sex and age-matched adults. Those with suspicion of secondary hypertension, renal disease, diabetes mellitus, chronic heart failure or other forms of cardiovascular diseases and pregnant women were excluded from both study groups.

Study protocol: The study population consisted of 88 individuals that included 44 patients with WCH and 44 normotensive controls; seen at the MOPD at the UITH during a 12-month period. All study participants had complete physical examination, standard 12-lead electrocardiography, ABPM and echocardiography. All eligible participants were informed about the study, and informed consent was obtained. Thereafter, each participant completed a self-administered questionnaire.

Sample technique: Consecutive sampling was used where 44 patients with WCH and 44 age and sex-matched participants were recruited.

Office BP Measurements: Office BP was taken in the office after a 5-minute rest with the participant seated, office BP measurements were taken with a mercury sphygmomanometer, and were taken on the bare arm that was supported and held at heart level. The mean of three (3) measurements was used as the office BP.

ABPM measurements: ABPM was performed using an oscillometric device (CONTEC®), which was revalidated regularly against a mercury sphygmomanometer. Thereafter, The ABPM was attached to each participant with the day-time measurements taken every 30 minutes as from 7 a.m. to 10.00 p.m. and thereafter, ABPM reads every one hour from 10:00 p.m. to 7.00 a.m. The participants were all instructed to engage

in their usual activities throughout the day. The appropriate cuff for arm circumference was placed on the non-dominant arm and the participants were instructed to keep their arm extended at cardiac level during automatic BP measurements. The guidelines of the European Society of Hypertension (ESH) for the treatment of hypertension's cut-off limits was applied, thus: normal day-time, mean 24-hour ABPM and night-time ABPM were 135/85mmHg, 130/80mmHg and 120/70mmHg respectively. (Mancia *et al.*, 2013).

Participants' categorization into subgroups on the basis of office BP and ABPM.

1. Normotensive individuals by both office and ABPM methods were referred to as truly normotensive individuals.
2. Individuals who were hypertensive by both methods were referred to as those with true hypertension.
3. WCH was defined as office BP <140/90mmHg despite a normal day-time ABPM <135/85mmHg.
4. Individuals with normal office BP but elevated BP on ABPM were described as those with masked white coat hypertension (WCH).

All study participants had resting echocardiographic study performed on them using an Aloka SSD-4000 (2004) echocardiography machine following the established standard technique and parameters by the American Society of Echocardiography (ASE) recommendations. (Henry *et al.*, 1980).

A two-dimensionally guided M-mode echocardiogram was performed on each participant at the same visit by a single Cardiologist, who was blinded to their BP status. Accurate linear measurements of interventricular septal wall thickness, posterior wall thickness, and LV internal dimensions, including end-diastolic/systolic diameters were obtained. Left ventricular mass index (LVMI) was calculated by Devereux's formula. (Devereux, 1987). The geometric classification was defined by the combination of increased relative wall thickness (RWT) and LVH (LVMI >115 g/m² for men, >95 g/m² for women) at end diastole. Ejection fraction, mitral pulse-wave Doppler E/A ratio (Em/Am), deceleration time, and isovolumetric relaxation time were estimated with two-dimensional (2-D) echocardiography.

Ethical consideration: Ethical approval was granted by the Ethical Review Committee of the University of Ilorin Teaching Hospital, Ilorin, Nigeria. Approval number: ERC PAN/2014/05/1302c.

Statistical analysis: Analysis of the data was done using SPSS 20. Quantitative and qualitative demographic characteristics were summarized and presented in tabular forms. Data were expressed as mean ± standard deviation (SD) while frequencies were expressed as percentages. The Student t-test was used to compare the means of continuous variables between two groups that were normally distributed. Chi-square was used to compare proportions. The results were presented as the odds ratio with corresponding 95% confidence interval. For all tests, statistical significance was set at a p-value < 0.05.

RESULTS

The demographic, anthropometric and clinical characteristics of the study population.

A total of 88 participants consisting of 44 patients with WCH and 44 age and sex-matched normotensive controls were studied. Twenty-seven (27) of the participants in each group were females. Age range for both groups was 18–75 years, the mean age was 43.3 ± 11.4 years and 43.6 ± 9.4 years for those WCH and control respectively. Participants with WCH had significantly higher weight, BMI, office SBP, and office DBP

All the ambulatory blood pressure of the WCH were significantly higher than the control group. However, the day-time pulse rate was similar in both groups, as shown in Table 2. The echocardiographic parameters in both groups were also similar. 24 of the WCH group and 19 of the control group had LVH, with no statistical difference between both groups, as shown in Table 3.

Table 1:

The demographic, anthropometric and clinical parameters of the study participants.

Variables	WCH (n=44)	Control (n=44)	P-values
Male, n	17	17	0.897
Female, n	27	27	
Age (years)	43.3±11.4	43.6±9.4	0.897
Weight (kg)	73.3±13.0	65.3±12.2	0.004*
Height (cm)	1.67±0.08	1.66±0.09	0.569
BMI (kg/m ²)	26.4±4.5	23.8±4.3	0.008*
WC (cm)	87.3±15.4	83.5±11.3	0.192
HC (cm)	97.9±13.3	96.1±10.2	0.492
Waist-Hip ratio	0.89±0.13	0.87±0.06	0.240
Pulse rate (bpm)	80.5±13.2	75.3±11.8	0.468
Office SBP (mmHg)	144.2±12.2	117.0±11.7	<0.001*
Office DBP (mmHg)	88.3±10.3	72.3±9.6	<0.001*

Key: * = Statistically significant, n = number, SD = Standard deviation, BMI = Body mass index, WC = Waist circumference, HC = Hip circumference, SBP = Systolic blood pressure, DBP = Diastolic blood pressure, b.p.m = beats per minute.

Table 2:

Ambulatory blood pressure indices of the participants with WCH and Control.

Variables	WCH (n=44)	Control (n=44)	P-values
24-hr SBP (mmHg)	123.3±5.9	116.9±7.7	<0.001*
24-hr DBP (mmHg)	73.0±5.1	69.1±6.8	0.003*
Day-time SBP (mmHg)	124.5±6.0	118.9±8.3	<0.001*
Day-time DBP (mmHg)	74.5±5.3	70.8±7.0	<0.001*
Night-time SBP (mmHg)	118.6±8.5	109.5±8.3	<0.001*
Night-time DBP (mmHg)	69.2±5.7	62.3±7.0	<0.001*
Day-time pulse rate (bpm)	79.4±9.2	79.4±9.2	0.988
Day-time pulse pressure (mmHg)	50.3±6.5	46.7±6.1	0.059

Key: * statistically significant, WCH, White coat hypertension; SBP, Systolic blood pressure; DBP, Diastolic blood pressure, n=number.

Table 3:

The echocardiographic parameters of the participants with WCH and normal blood pressure.

Variables	WCH (n=44)	Control (n=44)	P-values
AOD (cm)	2.83±0.23	2.77±0.32	0.374
LAD (cm)	3.36±0.54	3.34±0.47	0.888
LVDd (cm)	4.55±0.42	4.57±0.64	0.860
LVDs (cm)	2.90±0.34	2.93±0.57	0.800
LVM (g)	227.14±64.17	211.76±89.64	0.359
LVMI (g/m ²)	122.66±31.10	119.48±40.93	0.683
EF (%)	65.73±6.86	66.23±7.40	0.743
Mitral E/A	1.24±0.46	1.38±0.43	0.138
DT (ms)	183.02±71.41	196.23±79.07	0.113
IVRT (ms)	105.70±17.07	98.95±22.12	0.138
LVH, n	24	19	0.286

Key:

WCH, White coat hypertension;

SH, Systemic hypertension; SD, Standard deviation;

BP, Normal blood pressure; AOD, Aortic Opening dimension; LAD, Left atrial dimension; LVM, Left ventricular mass; LVMI, Left ventricular mass index;

RWT, Relative wall thickness; EF, Ejection fraction;

DT, Deceleration time; IVRT, Isovolumetric relaxation time, LVH, left ventricular hypertrophy.

DISCUSSION

This study showed high but similar prevalence of LVH in both the WCH and normotensive groups as 24 individuals with WCH and 19 of the normotensive individuals had LVH. Additionally, in this study, both WCH and normotensive groups showed similar cardiac structures, as there was no significant difference in their left ventricular mass, left ventricular mass index and left atrial diameter values. Previous studies on the association between white-coat hypertension and left ventricular hypertrophy (LVH) in WCH have shown conflicting results. (Cuspidi *et al.*, 2018, Huang *et al.*, 2017, Franklin *et al.*, 2013, Staessen *et al.*, 1999, Pierdomenico *et al.*, 1995, Parati *et al.*, 2000a). There has been documented evidence of intermediate risk of subclinical target organ damage between normotension and sustained hypertension. These findings are in tandem with the findings (Verdecchia *et al.*, 1999) that showed the prevalence of LV hypertrophy and LV mass were similar in their study population of with WCH and normotension. Another study equally showed similar cardiac structure in 18 normotensive and 18 white coat hypertensive individuals (White *et al.*, 1989). Also, white coat hypertensives were shown to have similar cardiovascular risk as their normotensive controls. (Hoegholm *et al.*, 1993). However, increased left ventricular mass index were reported among Nigerians with high normal BP in comparison with those with optimal BP (Saidu *et al.*, 2018). Also, the results of the recently performed meta-analyses provide evidence that white-coat hypertension is characterized, at cardiac level, by an increase in left ventricular mass index and greater values of left atrial diameter (Cuspidi *et al.*, 2015). Accounting for the different findings between these later studies and our study could be the relatively small sample size used in our study.

Worthy of note in our study, participants with WCH display increased body mass index which has also being

previously documented. (Brady, 2016, Dele-Ojo *et al.*, 2019). Metabolic alterations in combination with elevated office blood pressure and increased blood pressure variability contribute to the development of subclinical target organ damage at cardiac, vascular and renal level. (Sega *et al.*, 2001, Brady, 2016). This could account for the occurrence of LVH in our study population. Obesity is associated with LVH irrespective of blood pressure (Brady, 2016). Elevated BP has been implicated in the pathogenesis of left ventricular hypertrophy, however, the extent of cardiac growth and response to increased pressure loading is not similar among patients, thereby suggesting genetic mechanisms in cardiac hypertrophy (Simpson *et al.*, 1995). Blacks are known to have a greater left ventricular wall thickness and left ventricular mass, even with equivalent BP than White patients. (Sharp *et al.*, 2008). Furthermore, there were more women in our study population as this could account for the high percentage of LVH in both groups. Studies have shown that women with hypertension are at higher risk of developing LVH than their male counterparts with similar BP measurements (Liao *et al.*, 1995, Wassertheil-Smoller *et al.*, 2004). LVH in women is a strong cardiovascular risk factor as it causes an increased incidence in atrial fibrillation and sudden death in them. (Liao *et al.*, 1995, Wassertheil-Smoller *et al.*, 2004). The 2012 International Database on Ambulatory Blood Pressure in Relation to Cardiovascular Outcomes (IDACO) study also revealed that the incidence rate of cardiovascular events in participants with untreated WCH was no greater than in the untreated population with normotension. (Franklin *et al.*, 2012). The findings in this study are in tandem with other studies that showed that the level of target organ damage is no greater than in the normotensive control population. It will be nonetheless important to assess every patient with WCH for the presence of end organ damage such as LVH and to be followed up for the development of other cardiovascular risk factors. The PAMELA showed a significantly higher risk of new onset diabetes mellitus during a 10- year follow-up in untreated white coat hypertensives as compared with normotensive individuals (Hoegholm *et al.*, 1993) and 43% of WCH had progressed to sustained hypertension. (Sega *et al.*, 2001) Similarly, in Finland, the relative risk for developing sustained hypertension in WCH was almost three times greater than the one detected in the normotensive group (Hanninen *et al.*, 2012).

Therefore, if our study participants are followed up, there may be a significant difference in the cardiac structure of the WCH and the normotensive control. There is therefore need for patients' education as regard increased cardiovascular risks, with a special emphasis on maintaining optimal weight. In the absence of additional cardiovascular risk factors, intervention may be limited to lifestyle changes but should also include meticulous follow-up because people with WCH have a greater risk of progressing to SH (Hoegholm *et al.*, 1993).

In conclusion, there is high but similar prevalence of LVH among participants with WCH and normotension among adult Nigerians. Hence, there is need to assess every patient with WCH for the presence of LVH and to be followed up for the development of other cardiovascular risk factors.

Authors' contributions: DBF made substantial contributions to conception and design, acquisition, analysis and interpretation of data and was involved in drafting the manuscript and revising it critically for important intellectual content. OJA made substantial contributions to conception and design, acquisition, analysis and interpretation of data and was involved in drafting the manuscript and revising it critically for important intellectual content. OOD made substantial contributions to conception and design, acquisition, of data and was involved in revising the manuscript critically for important intellectual content. BHS made substantial contributions to conception and design, acquisition, of data and was involved in revising the manuscript critically for important intellectual content. KPM made substantial contributions to conception and design, acquisition, analysis and interpretation of data and was involved in drafting the manuscript and revising it critically for important intellectual content. KIA made substantial contributions to conception and design, analysis and interpretation of data and was involved in drafting the manuscript and revising it critically for important intellectual content. OABO made substantial contributions to conception and design, analysis and interpretation of data and was involved in drafting the manuscript and revising it critically for important intellectual content. All authors read and approved the final manuscript

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