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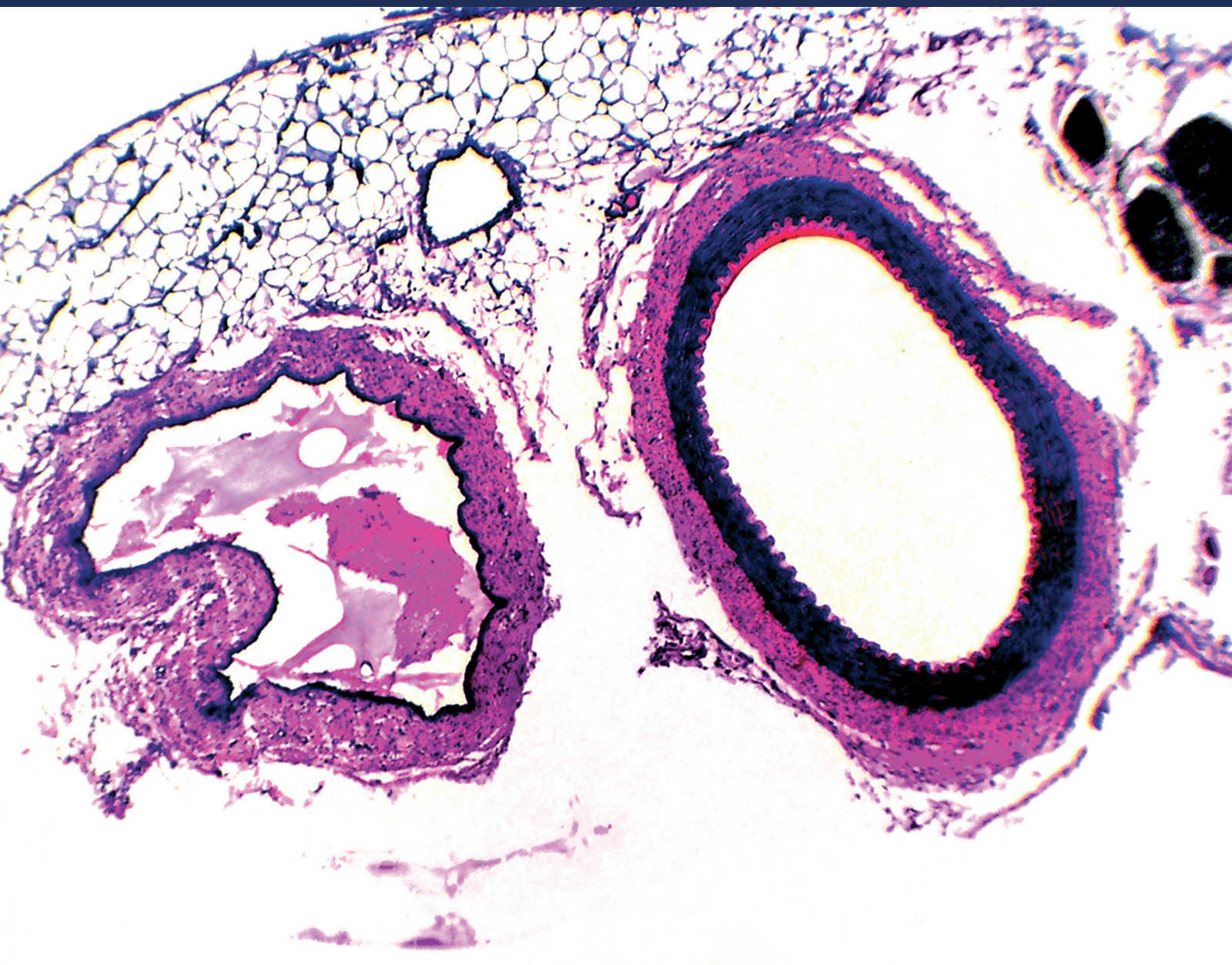
Sleep Disorders, Obesity, Hypertension, and Cardiovascular Risk

Guest Editors: Samy I. McFarlane, Olugbenga Ogedegbe, Amgad N. Makaryus, Charles Agyemang, and Girardin Jean-Louis



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Editorial

Sleep Disorders, Obesity, Hypertension, and Cardiovascular Risk

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The pandemic of obesity is associated with parallel epidemics of sleep disorders, diabetes, hypertension, and cardiovascular disease (CVD), that is, the primary cause of morbidity and mortality among adults [1]. Sleep disorders generally go unrecognized and undiagnosed and appear to play a major role in the interrelationships between obesity, diabetes, hypertension, and cardiovascular disease [2–4]. Accumulating evidence from cross-sectional as well as longitudinal studies by various groups, including ours, indicates close interrelationships among sleep disorders and diabetes, hypertension, and CVD including stroke, coronary artery disease, and heart failure, particularly among minority populations and women [2–5]. Postulated mechanisms or mediators of interrelationships between sleep disorders and CVD include oxidative stress, increased inflammation, increased uric acid endothelial dysfunction, dyslipidemia, and hypercoagulability, which are common underlying CVD risk factors among individuals with metabolic syndrome [6–8]. Furthermore, the cost of undiagnosed sleep disorders appears to be exceedingly high, prompting the American Academy of Sleep Medicine to recommend screening for at-risk individuals [9, 10]. This is quite important giving the mounting evidence of decreased CVD risk and improved cardiometabolic functions with treatment of sleep disorders, particularly among patients with sleep apnea [9].

In this special issue, we assembled a group of world-renowned editors with complementary expertise in sleep medicine, hypertension, diabetes, obesity, and cardiovascular disease to lead this initiative. Commensurate with level of expertise of the editorial team, we were able to attract important papers from established investigators from all over the world. Judging from the accepted papers for this special issue, we surmise that they are both topical and timely and they are likely to have a significant impact on the field.

The issue covers a wide range of topics, from dietary interventions, in the form of low glycemic index food and its effectiveness in lowering blood pressure to factors associated with medication nonadherence among hypertensives in two African countries: Ghana and Nigeria. Another important topic covered is the implications of renal denervation, a rather novel and increasingly studied potential therapy for hypertension, in patients with sleep apnea. An interesting topic also examined in a research paper indicated that in Black American working nonday time shift are more likely to report hypertension, especially with short sleep duration. This article opens further questions for investigations including those examining the underlying mechanisms for these findings. This special issue also included an epidemiologic assessment for the prehypertension and hypertension in two countries in Sub-Saharan Africa. This study assessed predictors of various stages of hypertension including obesity and educational levels in these vulnerable populations. Another closely related article from Africa among people with hypertension assessed the subtypes of hypertension in different light including

controlled hypertension, isolated systolic hypertension, and isolated diastolic hypertension as well as systolic-diastolic hypertension as they relate to obesity. This is quite important since different subtypes confer various degrees of risk. For example, among Blacks and/or people with diabetes systolic hypertension is predominant and is associated with high CVD risk factors including microalbuminuria, insulin resistance, postural hypertension, salt sensitivity, and volume expansion. Characterization of subtypes of hypertension not only opens the doors for further investigations of research questions, but also helps strategize in terms of treatment such as the utilization of low salt diet, diuretics, and agents that inhibit the renin angiotensin aldosterone function (RAAS), such as Angiotensin Converting Enzyme (ACE) Inhibitors and the Angiotensin Receptor Blockers (ARBs).

Finally, the interrelationships between sleep disorders and CVD are explained and illustrated in a well-written review article included in this issue that highlights the most recent findings and insights in this highly complex topic, providing the readers with food for thought that will hopefully generate testable and clinically important hypotheses.

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Olugbenga Ogedegbe
Amgad N. Makaryus
Charles Agyemang
Girardin Jean-Louis

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Research Article

Factors Associated with Medication Nonadherence among Hypertensives in Ghana and Nigeria

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Background. Blood pressure (BP) control is poor among hypertensives in many parts of sub-Saharan Africa. A potentially modifiable factor for control of BP is medication nonadherence (MNA); our study therefore aimed to determine factors associated with MNA among hypertensives in Ghana and Nigeria. *Methodology.* We conducted a multicenter cross-sectional study. Patients were recruited from Korle-Bu Hospital ($n = 120$), Ghana; and University of Port Harcourt Teaching Hospital, ($n = 73$) Apapa General Hospital Lagos ($n = 79$) and University College Hospital Ibadan ($n = 85$), Nigeria. *Results.* 357 hypertensive patients (42.6% males) participated. MNA was found in 66.7%. Adherence showed correlation with depression ($r = -0.208$, $P < 0.001$), concern about medications ($r = -0.0347$, $P = 0.002$), and knowledge of hypertension ($r = 0.14$, $P = 0.006$). MNA was associated with formal education ($P = 0.001$) and use of herbal preparation ($P = 0.014$). MNA was found in 61.7% of uninsured participants versus 73.1% of insured participants ($P = 0.032$). Poor BP control was observed in 69.7% and there was significant association between MNA and poor BP control ($P = 0.006$). *Conclusion.* MNA is high among hypertensives in Ghana and Nigeria and is associated with depression, concern about hypertensive medications, formal education, and use of herbal preparations. The negative association between health insurance and MNA suggests interplay of other factors and needs further investigation.

1. Introduction

Hypertension is a common but treatable public health problem globally. It is estimated to cause 7.5 million deaths annually, about 12.8% of all deaths worldwide [1]. Globally, the prevalence of hypertension in adults was approximately 40% in 2008 [2]. The number of people worldwide with hypertension rose from 600 million in 1980 to nearly 1 billion in 2008. The burden of hypertension is particularly high in sub-Saharan African countries. The reported prevalence of

hypertension in Ghana ranges from 19% to 32.8% in rural areas and 25.5 to 48% in urban areas [3–5]. Similarly, recent studies in Nigeria showed that the prevalence of hypertension in rural areas ranges from 21 to 25% [6, 7] while in semiurban and urban areas the prevalence ranged from 27 to 46% [8–11]. Optimal blood pressure (BP) control with levels below 140/90 mmHg is associated with significant reduction in cardiovascular complications such as stroke and coronary heart disease [12, 13].

The increasing rates of hypertension in sub-Saharan Africa have been attributed to rapid epidemiologic transition from an agrarian lifestyle to a more westernized lifestyle, with increasing rates of obesity, unhealthy diet, and physical inactivity [3, 14]. Blood pressure control is generally poor among hypertensive patients in sub-Saharan Africa, and efforts to improve BP control are needed. Poor BP control among hypertensives in sub-Saharan Africa is related to the complex interplay of patient, provider, and socioeconomic factors in this region [3, 14]. For example, patients may lack knowledge about hypertension, or they may harbour beliefs that are discordant with those of the traditional medical model regarding the causes and treatment of hypertension. As a result, patients' beliefs may be discordant with practices associated with BP control potentially leading to poor medication adherence. Additionally, patients may exhibit poor medication adherence because they are unable to afford the cost of medications. Similarly, healthcare providers may have insufficient time and resources to provide the necessary education and treatment.

Of the patient factors that affect BP control, poor medication adherence is the most salient and little studied in sub-Saharan African countries including Nigeria and Ghana. Medication nonadherence (MNA) is a potentially modifiable risk factor for the improvement of BP control. Factors that may influence adherence include socioeconomic status, access to health insurance, depression, patient's knowledge of the disease, and beliefs about medications [15]. Past studies have reported a wide range of MNA in Ghana and Nigeria from 17.4 to 93%, making it difficult to compare the degree and factors associated with MNA in both countries [16–24].

In order to address these significant gaps in the adherence literature in sub-Saharan Africa, our study documents the levels and factors associated with MNA among hypertensive patients in the hospital setting in Ghana and Nigeria.

2. Methods

In this multicenter cross-sectional study, patients were recruited from four hospitals: Korle-Bu Hospital (n = 120), Ghana, and University of Port Harcourt Teaching Hospital, (n = 73) Apapa General Hospital Lagos (n = 79), and University College Hospital Ibadan (n = 85), Nigeria. Patients were eligible to be in this study if they were aged 18 years or older, were diagnosed hypertensive, and had been placed on medication for at least twelve months and provided informed consent. Hypertension was defined as systolic BP of ≥140 mmHg and/or diastolic BP of ≥90 mmHg [25] or patients already under treatment with antihypertensive medications. Patients were recruited from general outpatient or specialist medical clinics. The questionnaires were administered by the authors or trained research assistants. At each site, each consecutive patient who met the inclusion criteria was recruited. The same recruitment procedure was used in each center. Patient recruitment into the study took place between April and September 2013. Data collection was conducted by the authors and trained research assistants at each study site using a structured questionnaire. Blood pressure was measured with an Omron electronic BP machine, after at least 10 minutes rest, in the dominant arm of seated patients on three occasions at an interval of one minute. The average of the last 2 readings was recorded.

The dependent variables were medication adherence and BP control. Adherence to antihypertensive medications was measured using the 8-item Morisky medication adherence scale. Based on a pilot study in Korle Bu Ghana, the response options for the Morisky scale were modified from "never/rarely," "once in a while," "sometimes," "usually," and "all the time" to "Never/rarely" versus "sometimes/usually/all the time." Individual item scores were summed and those with a score of 8 were considered adherent to medication. Medium adherence corresponded to a score of 6–8, while a score of <6 was considered low adherence [26]. Medication nonadherence referred to a score of <8 (i.e., medium or low adherence). Blood pressure control was defined as systolic BP < 140 mmHg and diastolic BP < 90 mmHg [27].

Demographic and socioeconomic characteristics including age, gender, ethnicity, education, occupation, and income were recorded. Educational status was classified as none, primary, junior secondary, senior secondary, and tertiary. Monthly income was stratified as <$100, $101–300, $301–1000, $1001–3000, and >$3000. Clinical information regarding when the diagnosis of hypertension was made, for how long patients had been on antihypertensives, and presence of any associated comorbid conditions were obtained from patients' medical records. Beliefs about medication were measured using the modified beliefs about medication questionnaire (BMQ) [28]. The BMQ includes questions on beliefs about the necessity of taking medications (BMQ-necessity) and concerns about medications (BMQ-concern). The difference between the BMQ-necessity and BMQ-concern scores was also determined for each patient (BMQ necessity-concern score). Each question on the BMQ is based on a 5-point Likert scale with response options: "strongly agree," "agree," "disagree," "strongly disagree," and "uncertain." Pilot testing of the BMQ indicated that participants were more comfortable with 3 response options. We therefore modified the responses to "agree," "disagree," and "uncertain," The parameters were scored as disagree = 1, uncertain = 2, and agree = 3. The sum total of the BMQ-necessity score, BMQ-concern, and the difference between BMQ-necessity and concern scores was calculated [28]. The Patient Health Questionnaire 9 (PHQ-9) was used to assess depression in this study. For this scale, sores of 0, 1, 2, and 3 are assigned to response categories of "not at all," "several days," "more than half the days," and "nearly every day," respectively. The PHQ-9 total score ranges from 0 to 27. PHQ-9 scores of 0–4, 5–9, 10–14, 15–19, and 20–27 represent none to minimal, mild, moderate, moderately severe, and severe depression, respectively. Scores of >4 were

classified as depression. A 17-item questionnaire based on the JNC 7 and adapted from previous studies was used to assess knowledge of hypertension [14, 29–31]. The questions were based on true or false responses to statements such as "high blood pressure cannot be cured but can be controlled," "high blood pressure can damage hearts," "a person who has high blood pressure should take more salt," and "management of high blood pressure must include medications, diet, and lifestyle modification." A score of 1 mark was given for each correct response and the final score was a sum total of the correct responses.

Data collected was entered into Statistical Package for Social Sciences (SPSS) software student version 17.0 and used for analysis. Descriptive statistics such as means, standard deviations, proportions, and percentages were used to summarize quantitative and qualitative variables, respectively. Inferential statistics including Chi-square analysis and Pearson's correlation were used to compute associations between variables. The student t-test was used to compare means. P values < 0.05 were considered significant and r-values of >0.15 were considered strong correlations. Ethical approval for the study was obtained from University of Ghana Ethical and Protocol Review Committee (EPRC), the University of Ibadan/University College Hospital Ibadan Ethical Review Committee, and the University of Port Harcourt Ethical Review Committee.

3. Results

As shown in Table 1, a total of 357 hypertensive patients were recruited for the study, of which 42.6% were men. Their mean age was 56.6 ± 13.2 years. The majority of the study participants (33.61%) were recruited from Korle Bu, while 20.4%, 22.1%, and 23.8% participants were recruited from Port Harcourt, Apapa, and Ibadan, respectively. There were significant differences in the age of participants, gender, and access to health insurance between sites. The cohort from Korle Bu had the highest proportion of females and participants who were more likely to have health insurance.

Nonadherence to medications was present in 66.7% of participants. Port Harcourt had the highest prevalence of MNA (95.9%), while Ibadan had the lowest (45.1%). Depression was present in 31.4% of the study participants, with 2.8% and 1.4% reporting moderately severe and severe depression, respectively. Depression was more prevalent in the cohort from Korle Bu (41.7%) and Port Harcourt (41.1%) compared to the other centres. Table 1 shows the distribution of patient characteristics by site.

3.1. Relationship among Depression, Beliefs about Medicines, and Medication Adherence. The mean age of patients who were nonadherent to medications was 54.5 ± 13.2 years while those who were adherent had a mean age of 60.9 ± 12.1 years ($P < 0.001$). Among the cohort from Korle Bu, those who were nonadherent were also significantly younger than subjects who were adherent, 55.3±13.4 years versus 61.3±13.7 years ($P = 0.037$). There was significant correlation between PHQ-9 score for depression and Morisky score in Korle Bu ($r = -0.230$, $P = 0.012$) and in the pooled data ($r = -0.203$, $P < 0.001$). The mean BMQ-concern score among participants who were nonadherent was 9.0 ± 2.7 compared to 7.5 ± 2.5 among those who were adherent. There was a significant negative correlation between BMQ-concern score and Morisky score in Ibadan ($r = -0.338$, $P = 0.002$) and in the pooled data ($r = -0.355$, $P = 0.000$). The BMQ-necessity-concern score was associated with MNA in the pooled data ($r = 0.336$, $P < 0.001$). Knowledge of hypertension was significantly but weakly correlated with Morisky score ($P = 0.006$, $r = 0.14$). Table 2 shows correlations among Morisky score and depression, beliefs about medication, knowledge of hypertension, and income by site.

3.2. Relationship among Socioeconomic Status, Income, Health Insurance, and Medication Adherence. Level of income did not show correlation with Morisky score ($r = 0.021$, $P = 0.744$). The majority of participants (56.3%) did not have any health insurance. MNA occurred in 47.7% of those who did not receive formal education compared with 70.9% of those who had some form of formal education ($P = 0.001$). MNA was noted in 61.7% of those who did not have health insurance and in 73.1% of those who had health insurance ($P = 0.032$). MNA was significantly more common among patients who used herbal preparation for the treatment of systemic hypertension ($P = 0.014$). There were no differences in medication adherence between patients who were married compared with those who were not. See Table 3 for a summary of characteristics by adherence.

3.3. Correlations of Blood Pressure Control. Blood pressure was controlled in 35.9% of study participants. There was variation in the proportion of patients with BP control across the study sites ranging from 9.6%, in Port Harcourt, to 54.1% in Ibadan. There was significant association between medication nonadherence and poor BP control in the pooled data ($P = 0.006$). Table 1 includes rates of BP control and medication adherence across sites. The cohort of patients from Port Harcourt had the highest level of MNA (95.9%) and the lowest proportion with BP control (9.6%, $n = 4$).

4. Discussion

We report a high prevalence of MNA (66.7%) among hypertensives in hospitals in Ghana and Nigeria. Patients who were nonadherent were significantly younger than patients who were adherent. There was significant negative correlation between depression and concerns about medication and medication nonadherence. Knowledge of hypertension was positively correlated with adherence. Patients who were adherent were less likely to use herbal preparations or to have received formal education and were more likely to have children. Level of income was not associated with adherence. Not unexpectedly, poor BP control was significantly associated with MNA. Access to health insurance surprisingly showed significant association with MNA. The proportion of patients who had uncontrolled BP was higher among patients who had health insurance, compared to patients without health insurance, but the finding was not significant. Further studies on the operation of the health insurance system are

Table 1: Distribution of study population characteristics by site.

Parameter	Korle Bu	P. Harcourt	Lagos	Ibadan	Pooled
Total (%)	120 (33.6)	73 (20.4)	79 (22.1)	85 (23.8)	357 (100)
Age (years)[a]	57.0 ± 13.7	47.4 ± 12.5	57.8 ± 9.8	62.9 ± 11.5	56.6 ± 13.2
Females (%)[a]	70 (58.3)	37 (50.7)	56 (70.9)	42 (49.4)	205 (57.5)
Insurance *N* (%)[a]	114 (95)	20 (27.4)	5 (6.3)	17 (20)	156 (43.7)
HTN with comorbidities (%)[a]	57.4	20.5	34.2	62.4	45.8
Depression (%)					
No (%)	70 (58.3)	43 (58.9)	60 (75.9)	72 (84.7)	245 (68.6)
Mild (%)	32 (26.7)	18 (24.7)	18 (22.8)	10 (11.8)	78 (21.8)
Moderate (%)	10 (8.3)	5 (6.8)	1 (1.3)	3 (3.5)	19 (5.3)
Mord-severe (%)	4 (3.3)	6 (8.2)	—	—	10 (2.8)
Severe (%)	4 (3.3)	1 (1.4)	—	—	5 (1.4)
Total (%)	**120 (100)**	**73 (100)**	**79 (100)**	**85 (100)**	**357 (100)**
BMQ-necessity [median (IQR)]	14 (11–15)	11 (9–13)	15 (13–15)	10.5 (7–13)	
BMQ-concern [median (IQR)]	7.5 (5–11)	11 (9–12.5)	7 (8-9)	7 (5–9)	
Knowledge about HTN [median (IQR)]	15 (14–16)	13 (11–14)	13 (12–15)	14 (13–15)	14 (13–15)
Nonadherence (%)	72.5	95.9	53.2	45.9	66.7
Medium adherence (%)	41.7	12.3	38.0	32.9	32.8
Low adherence (%)	30.8	83.6	15.2	12.9	33.9
Blood pressure control (%)[a]	27.7	9.6	53.2	54.1	35.9
Educational status					
None (%)	6.7	1.4	53.2	16.5	18.2
Primary (%)	7.5	31.5	19.0	21.2	18.2
Junior secondary (%)	31.7	12.3	8.9	1.2	15.4
Senior Secondary (%)	15.0	28.8	13.9	18.8	18.5
Tertiary (%)	39.2	26.0	5.1	42.4	29.7
Occupation[a]					
Petty trader (%)	24.6	12.3	45.5	13.1	23.9
JCS (%)	23.7	19.2	6.5	3.6	14.2
SCS (%)	11.0	15.1	2.6	14.3	10.8
Businessman (%)	11.0	20.5	22.1	17.9	17.0
Unemployed (%)	4.2	5.5	15.6	1.2	6.3
Housewife (%)	0.8	9.6	0	1.2	2.6
Others (%)	1.7	9.6	2.6	0	3.1
Artisans (%)	5.9	0.0	1.3	7.1	4.0
Retired (%)	16.9	8.2	3.9	41.7	18.2
Use of herbal preparation (%)[a]	15.8	35.6	11.7	9.4	17.5

[a] $P < 0.005$.

BMQ: beliefs about medication questionnaire; IQR: interquartile range; HTN: hypertension; JCS: junior civil servant; P. Harcourt: Port Harcourt; SCS: senior civil servant.

warranted while measures to improve medication adherence are required.

We report a high prevalence of MNA in our study population (66.7%), but our finding is within the range of MNA that has been documented in previous studies from sub-Saharan Africa. Most studies in Nigeria and Ghana have documented MNA ranging from 32.7 to 49.3% [16, 17, 20, 23]. There was however a study from Ghana that documented MNA of 93% before the availability of National Health Insurance [19]. Elsewhere in sub-Saharan Africa, MNA ranged from 10.3 to 87.5% [32–38]. Variation may be partly due to the different definitions or methods used to assess MNA. Most of the studies though based on self-report, utilized different definitions for MNA. An advantage of our study was that the same tool was used to assess MNA in the various sites. Furthermore we also observed significant association between MNA and BP control in our study which will further validate the tool that was adopted to assess MNA in our study.

Our study found significant correlation between beliefs about medication and adherence to antihypertensives. Patients who had concerns about antihypertensive medications were less likely to be adherent to their medications. These findings are consistent with previous studies on the relationship between medication adherence and beliefs about

Table 2: Correlation of medication adherence (Morisky score) with depression, beliefs about medication, knowledge of hypertension, or income by site and in the pooled data.

Parameter	Korle Bu		Port Harcourt		Lagos		Ibadan		Pooled	
	r	P	r	P	r	P	r	P	r	P
Depression (PHQ-9)	−0.230	0.012	0.051	0.667	−0.043	0.705	−0.035	0.749	−0.203	0.000
BMQ-necessity	0.142	0.124	−0.079	0.507	0.091	0.433	0.002	0.984	−0.087	0.103
BMQ-concern	−0.148	0.111	−0.286	0.014	−0.014	0.905	−0.336	0.002	−0.355	0.000
BMQ-necessity-concern	0.215	0.020	0.174	0.141	0.079	0.505	0.210	0.060	0.337	0.000
Hypertension knowledge scale	0.024	0.797	0.212	0.071	0.019	0.865	−0.030	0.783	0.144	0.006
Income	0.139	0.143	−0.057	0.634	−0.200	0.081	0.099	0.419	−0.067	0.226

BMQ-concern: beliefs about medication concern score; BMQ-necessity: beliefs about medication necessity score; BMQ-necessity-concern: beliefs about medication necessity-concern score; $P = P$ value; r = Pearson's correlation coefficient.

medications [39]. Specifically, patients in our study had concerns about potential adverse effects of long term use of antihypertensives or felt that daily use of antihypertensive medications was a significant disruption of their lifestyles. Patients were also concerned that they may be becoming too dependent on their medications. Other studies have identified side-effects of antihypertensive medications as a reason for MNA in patients [19, 23, 35, 38]. Studies have also documented that forgetting to take medications is an important barrier to adherence [17, 23, 38]. In addition, adherence is usually better with medications that require less frequent administration [16, 36–38]. Health education specifically about antihypertensive medications including potential side-effects, and inquiry about side-effects the patient may be experiencing and use of medications that are associated with fewer side effects may lead to improvement in adherence. In addition, use of medications that do not cause more disruption of the patients' daily activities than necessary may also improve adherence.

Our study also found that depression was significantly associated with MNA, particularly among patients at Korle Bu, but also in the pooled data. To the best of our knowledge this study is the first to assess depression and MNA among hypertensives in sub-Saharan Africa. Depression has been associated with poor BP control and medication nonadherence in studies outside sub-Saharan Africa [40, 41]. In a study from the USA, antidepressants were associated with significantly longer initial persistence of antihypertensive therapy among patients with depression who developed hypertension [42]. Evaluation for depression and appropriate management of the depression may improve medication adherence among hypertensives in sub-Saharan Africa.

Patients who were not adherent were significantly younger than patients who were adherent. This pattern has been observed in adherence studies carried outside sub-Saharan Africa and has also been documented in Sub-Saharan Africa [26, 43, 44]. The reason for worse medication non adherence in younger patients is not clear. A potential reason may be that younger patients are not as concerned about their health compared with the older patients. Health education directed towards younger age group may improve outcomes among the younger patients.

Our study found positive and significant correlation between knowledge of hypertension and adherence to medications. Previous studies from Africa have associated lack of knowledge regarding the curability of hypertension and lifelong need for antihypertensives with MNA [18, 20, 23, 38]. Our data thus support the need for adequate health education on hypertension to improve MNA in the subregion. Furthermore, patients who reported using herbal preparations for the treatment of hypertension were more likely to show MNA. This is consistent with most studies on hypertension from sub-Saharan Africa that have associated the use of alternative medical therapy with MNA [17, 18, 20, 36, 38].

Studies from Nigeria have noted increasing adherence with increasing educational status but these associations were not significant [16, 23]. Literacy has also been associated with a higher BP control in Nigeria but this was also not significant [45]. Our study, however, found that patients who had received any form of formal education were more likely to show MNA than those who did not. It may be that educated participants in our study were more skeptical towards the use of antihypertensives. A similar observation was noted in a Ghanaian study which also found significant negative association between educational status and medication adherence [17]. Another study from the United States found higher adherence among men with lower levels of education than among more highly educated men [46]. Our data is consistent with a previous suggestion that health education on hypertension and its treatment should be provided for all hypertensive patients in our subregion irrespective of the patients' educational status [47].

In most studies from sub-Saharan Africa participants have identified inability to afford the cost of medications as an important barrier to medication adherence [17–19, 33, 36, 38]. A positive relationship between cost and MNA has also been found in studies outside of Africa [39] Studies have however not consistently demonstrated association of medication adherence with level of income. Our study did not find an association between MNA and income [23, 39, 43].

Table 3: Distribution of study population characteristics by adherence ($N = 357$).

Population Characteristics	Nonadherent N (%)	Adherent N (%)	P value
Gender			0.623
Male	104 (68.4)	48 (31.6)	
Female	134 (65.4)	71 (34.6)	
Study Site			<0.001
Korle-Bu	87 (72.5)	33 (27.5)	
Port Harcourt	70 (95.9)	3 (4.1)	
Lagos	42 (53.2)	37 (46.8)	
Ibadan	39 (45.9)	46 (54.1)	
Age	54.4 ± 13.2 years	60.9 ± 12.1 years	0.000
Educational status			0.006
None	31 (47.7)	34 (52.3)	
Primary	48 (73.8)	17 (26.2)	
Junior	42 (76.4)	13 (23.6)	
Secondary	47 (71.2)	19 (28.8)	
Tertiary	70 (60.6)	36 (34.0)	
Formal education			0.001
Yes	207 (70.9)	85 (29.1)	
No	31 (47.7)	34 (52.3)	
Marital status			0.967
Married	172 (66.9)	85 (33.1)	
Not married	66 (66)	34 (34)	
Children			0.04
Yes	217 (65.2)	116 (34.8)	
No	21 (87.5)	3 (12.5)	
Occupation			0.317
Employed	176 (68.5)	81 (38.5)	
Unemployed	59 (62.1)	36 (37.9)	
Cost of drug ($)			0.1
<10	58 (73.4)	21 (26.6)	
11–30	87 (65.9)	45 (34.1)	
31–50	36 (67.9)	17 (32.1)	
51–100	27 (69.2)	12 (30.8)	
>100	14 (45.2)	17 (50.8)	
Insurance			0.032
Yes	114 (73.1)	42 (26.9)	
No	124 (61.7)	77 (38.3)	
Use of herbal medication			0.014
Herbal med.	50 (80.6)	12 (19.4)	
No herbal med.	186 (63.5)	107 (36.5)	
Hypertension			0.006
Control	72 (56.7)	55 (43.3)	
Uncontrolled	163 (71.8)	64 (21.2)	
Comorbidities			0.874
No comorbidity	132 (69.8)	57 (30.2)	
DM or renal comorbidities	62 (62.6)	37 (37.4)	
Other comorbidities	38 (69.8)	23 (30.2)	

DM: diabetes mellitus.

One explanation may be that in many African studies, as in ours, only a negligible number belong to the high socioeconomic class, making it difficult to access MNA in the high socioeconomic class [23, 45]. On the other hand the lack of association between income and MNA may reflect an interplay of other factors that contribute to medication adherence. A study carried out in Nigeria in a setting in which antihypertensives were offered for free, noted that BP control was low though higher than in settings where medications were not given for free suggesting that MNA may not be entirely due to cost [48].

We found that access to National Health Insurance was significantly associated with MNA. In addition, BP tended to be higher in patients with access to health insurance than those who did not. Most of the patients who had access to National health Insurance were from Ghana. The Ghanaian patients also had the highest proportion of patients with depression and the depression may have contributed to the high proportion of patients with MNA in the Ghanaian patients in spite of the access to health Insurance. In addition, the way the health insurance system operates may also be contributory. In Ghana for instance, a three-month prescription from clinicians is usually dispensed in three tranches where patients are given a one month supply and asked to come back for refill of their medications for the other two months. Some patients do not return for refill of their medication because of lack of travel funds or lack of a system to remind them to go for the refill. This argues in favour of a critical review of the current national health insurance system in Ghana. Esunge and colleagues in Cameroon had suggested that factors that improved MNA among hypertensives in low resource settings were free medications, free hospital visits, free transportation, open discussion with medical staff, use of common dialects, and politeness of medical staff [49].

Another method that may contribute to improvement in medication adherence in low resource settings is the use of phone technology. Use of text messages has been associated with improvement in adherence to medications [50]. Use of phone technology reminders even in low resource settings may be useful in improving medication adherence in a large number of patients.

Strengths of our study include the multicenter nature of the study, and the use of uniform tools to assess medication non-adherence, depression, knowledge of hypertension, and beliefs about medication across the sites. Limitations of our study are that the study is hospital-based and most patients were from tertiary health centers. As such, the patients in our study are likely to have more comorbidities and to be more highly motivated than patients in the community. Therefore, proportion of patients who are non-adherent in the community may be higher than the observation in our study. Furthermore, MNA was assessed by verbal report and this may also potentially underestimate adherence because of recall bias or social desirability bias, and this may also apply to the other self-report measures. A more objective measure such as urine antihypertensive drug assay, may have demonstrated a higher degree of MNA. However, the study provides valuable information on the burden of MNA among hypertensives and the potential influence of factors such as beliefs about medications, depression, and health insurance on MNA.

5. Conclusion

We studied MNA among hypertensives in hospitals in Ghana and Nigeria. MNA was found in 66.7% of participants. MNA occurred in younger patients and in patients who had varying degrees of depression or were concerned about their medications. Knowledge of hypertension was positively and significantly correlated with adherence. MNA was associated with use of herbal preparations, and formal education. Expectedly adherence was significantly associated with BP control. We also found that MNA was associated with health insurance, and this may be related to either underlying depression or the mode of operation of the health insurance. The finding of significant association between health insurance and MNA underscores the need for studies to identify the underlying causes of this association. Treatment of depression in patients with hypertension and depression may improve outcomes. Patients irrespective of educational status need education concerning treatment of hypertension and side-effects of medication in addition to education on hypertension to improve MNA. Other methods to improve medication adherence such as use of phone technology should also be studied.

Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

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Research Article

Low-Glycemic-Index Foods Can Decrease Systolic and Diastolic Blood Pressure in the Short Term

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Background. We aimed to compare the effects of low- and high-GI foods on 24-hour ambulatory blood pressure. *Methods*. This longitudinal study was performed on 30 women, aged 18 to 40 years, during 24 hours. In the first leg of study all recruited subjects were assigned to LGI period for 24 hours and, after a 2-week washout period, all subjects were assigned to HGI period. BP was measured every hour during the 24-hour monitoring. *Results*. After the intervention, there were significant decreases in SBP and DBP in the LGI period (102.26±14.18 mmHg versus 112.86±9.33 mmHg for SBP and 66.96±10.39 mmHg versus 74.46±7.61 mmHg for DBP) ($P = 0.00$ and $P = 0.002$, resp.). However, in the HGI period, there was no significant change in SBP or DBP (110.66 ± 9.85 versus 111.80 ± 9.57 for SBP and 71.16 ± 9.16 versus 74.26 ± 10.09 for DBP) ($P = 0.6$ and $P = 0.06$, resp.). *Conclusion*. The results suggest that LGI foods may be beneficial in reducing 24-hour BP.

1. Introduction

High blood pressure (BP) is defined as systolic BP (SBP) ≥ 140 mmHg and/or diastolic BP (DBP) ≥ 90 mmHg. High BP is an independent risk factor for cardiovascular diseases, stroke, and kidney diseases. It is also one of the most common health problems worldwide [1].

As previous studies indicate, several dietary factors such as increased salt intake, insufficient potassium, obesity, overweight, excess alcohol intake, and high consumption of carbohydrates (CHO) including sugars and soft drinks can increase BP [2, 3]. However, total CHO intake has not been consistently associated with either increased or decreased BP. Differences in the type and source of dietary CHO may have various impacts on the relationship between CHO intake and BP [4].

Prevention of elevated BP is an important public health issue with the aim of reducing the overall disease rate, caused by hypertension [1]. In fact, reduced BP could have significant impacts on cardiovascular diseases, morbidity, and mortality [5].

Glycemic index (GI) provides a numeric classification of CHO foods, based on their glycemic response that reflects the rise in postprandial glycemia [6]. As previous studies have revealed, changes in SBP and DBP are associated with glycemic load (GL) and GI [3, 7, 8]. For instance, Philippou et al. in a study performed in 2009 found that a 6-month intensive lifestyle modification including dietary GI manipulation, in addition to healthy eating and weight loss, affects arterial compliance and 24-hour BP, which are risk factors for coronary heart disease (CHD). Low-GI (LGI) food has been suggested to be more effective in reducing CHD risks including pulse wave velocity and 24-hour BP [6].

However, previous studies have not considered factors such as obesity and family history of hypertension [3, 6, 8, 9]. Also, since participants differed from nonparticipants in terms of characteristics such as age, weight, height, ethnicity, and body mass index (BMI), the possibility of selection bias, which limits the generalization of the results, has not been ruled out.

In the present study, we hypothesized that 24-hour LGI foods would significantly decrease 24-hour ambulatory BP.

Table 1: Details and ingredients of consumed foods in 24-hour LGI period.

Food	Amount of intake	Carbohydrate (gr)	Protein (gr)	Fat (gr)	Calories (k cal)	%GI	GL (gr)
Special k	100 gr	79	9	1.5	375	54	11
Milk (3% fat)	500 cc	24	16	15	300	21	3
Oil	45 gr	0	0	45	405	0	0
Spaghetti	480 gr	192	12	0	800	42	20
Tomato sausage	30 gr	5	0	0	30	0	0
Total	—	**300**	**37**	**61.5**	**1910**		**34.1**
% of total calories		75.3%	9.3%	15.4%			

Table 2: Details and ingredients of consumed foods in 24-hour HGI period.

Food	Amount of intake	Carbohydrate (gr)	Protein (gr)	Fat (gr)	Calories (k cal)	%GI	GL (gr)
Corn flakes	50 gr	39.5	4.5	0.75	187.5	92	24
Milk (3% fat)	250 cc	12	8.25	7.5	150	21	3
Oil	45 gr	0	0	45	405	0	0
Rice	360 gr	162	9	0	660	84	45
Potato	300 gr	54	6	0	240	98	26
Tomato sausage	30 gr	5	0	0	30	0	0
Baguette	90 gr	66	9	0	240	108	24
Honey	30 gr	26	0	0	120	78	10
Total	—	**364.5**	**36.75**	**53.25**	**2032**		**132**
% of total calories		80%	8%	12%			

The aim of our study is assessing the effect of changing GI of foods on 24-hour BP.

2. Materials and Methods

2.1. Subjects. In this longitudinal study, subjects' demographic information including age, gender, weight, and height was gathered before the study. Overall, 30 women, aged 18–40 years, were selected based on BP level (below 140/90 mmHg).

The inclusion criteria were as follows: (1) SBP < 140 mmHg; (2) DBP < 90 mmHg; (3) nonuse of medications during the intervention; and (4) no drug therapy for hypertension.

The exclusion criteria were as follows: (1) diabetes; (2) prior history of diseases affecting BP (e.g., renal and cardiac diseases); (3) pregnancy and/or lactation; (4) vigorous physical activity during the intervention; (5) smoking; and (6) BP traces that were missing >4 hourly means over the 24 h.

All procedures involving human subjects were approved by the Research Ethics Committee of Mashhad University of Medical Sciences. Written informed consents were obtained from all the subjects. A checklist including demographic data and questions related to the inclusion criteria was completed by all participants at baseline.

2.2. Study Procedure. In the first leg of study all recruited subjects were assigned to LGI period for 24 hours and, after a 2-week washout period, all subjects were assigned to HGI period. The subjects were asked to only consume the determined foods. The participants maintained their usual diet and lifestyle during a washout period. A dietitian counseled the participants during 24 hours of intervention to ensure adherence to diets. The subjects were controlled in an isolated location and monitored by the dietitian for 24 hours. The designated foods were consumed by the subjects at the determined hours. Also, full and timely consumption of foods was controlled by the dietitian.

In our study, the energy intake of diets was similar in the two groups (1900–2000 k cal). Also, macronutrient distribution was equivalently prescribed in the two groups (75–80% CHO, 8-9% proteins, and 12–15% fat). The amounts of fat and protein in the diets were below the standard recommended levels since our study focused on foods rich in CHO for a better analysis of the effect of CHO on BP.

GI values were extracted from the International Tables of GI and GL and Values reference scale based on GI glucose = 100 [7]. Dietary GL was calculated as the product of dietary GI and CHO intake divided by 100. The daily dietary GL of each subject was calculated and summed up, and the GI of the whole diet was calculated, using the following formula (see [3]):

$$\frac{\text{dietary GL}}{\text{total available CHO intake in the day}} \times 100\%. \quad (1)$$

Tables 1 and 2 show details and ingredients of consumed foods in 24-hour LGI and HGI periods. Total 24-hour dietary GL of each subject was 34.1 gr for LGI period and 132 gr for HGI period. The daily dietary GI of each subject was 42.76% for LGI period and 84.46% for HGI period.

Fasting blood samples (after 12 hours of fasting and avoiding alcohol and exercise for 24 hours) were obtained at baseline to exclude diabetic cases from the study.

Table 3: Baseline characteristics of participants.

Variables	Percentage	Frequency
Age (years)		
18–20	10	3
20–25	53.3	16
25–30	33.3	10
30–35	3.3	1
BMI		
Underweight (BMI < 18.5 kg/m^2)	6.7	2
Normal weight (BMI = 18.5–24.9 kg/m^2)	83.3	25
Overweight (BMI = 25–29.9 kg/m^2)	10	3
Obese (BMI > 30 kg/m^2)	0	0

BMI: body mass index.

2.3. BP Screening. For screening BP, a cuff was fitted to the participants' nondominant arm by a trained nurse and removed after 24 hours. BP and heart rate (HR) were measured every hour during the 24-hour monitoring, providing a total of 24 readings within 24 hours. Subjects were instructed to immobilize their arms during cuff inflation. A wrist stabilizer was used to support the arm to ensure the best possible positioning of the device and minimize movements.

The patients were instructed to follow their routine daily activities and avoid any vigorous exercises, alcohol use, smoking, and use of medications while wearing the cuff. BP traces that were missing more than 4 hourly means over the 24 hours were excluded from the analysis.

2.4. Statistical Analysis. Statistical analyses were performed by SPSS version 11.5. First, Kolmogorov-Smirnov test was performed to assess the normality of quantitative variables. Data were presented as mean ± SD. Paired t-test was used for comparing variables before and after the intervention in each group and within groups. P values less than 0.05 were considered statistically significant.

3. Results

The current study was conducted on 30 female subjects, with the mean age of 24.63 ± 3.20 years (minimum of 18 and maximum of 32 years), mean weight of 57.16 ± 9.07 kg (minimum of 39 and maximum of 75 kg), mean height of 162.83 ± 6.11 cm (minimum of 150 and maximum of 178 cm), and BMI of 21.47 ± 2.60 kg/m^2 (minimum of 17.26 and maximum of 27.55 kg/m^2).

Table 3 shows the baseline characteristics of study subjects. According to this table, most of the participants (53.3%) were within the age range of 20–25 years. Overall, 6.7% of participants were underweight (BMI < 18.5 kg/m^2), 83.3% had a normal weight (BMI = 18.5–24.9 kg/m^2), and 10% were overweight (BMI = 25–29.9 kg/m^2); none of the participants were obese (BMI < 30 kg/m^2).

3.1. Blood Pressure (BP). The total values of 24-hour SBP and DBP in the LGI group were 73,559 mmHg and 47,390 mmHg, respectively. Also, the total values of 24-hour SBP and DBP in the HGI group were 73,546 mmHg and 47,929 mmHg, respectively. These numbers are the sum of mean blood pressure readings for each time point.

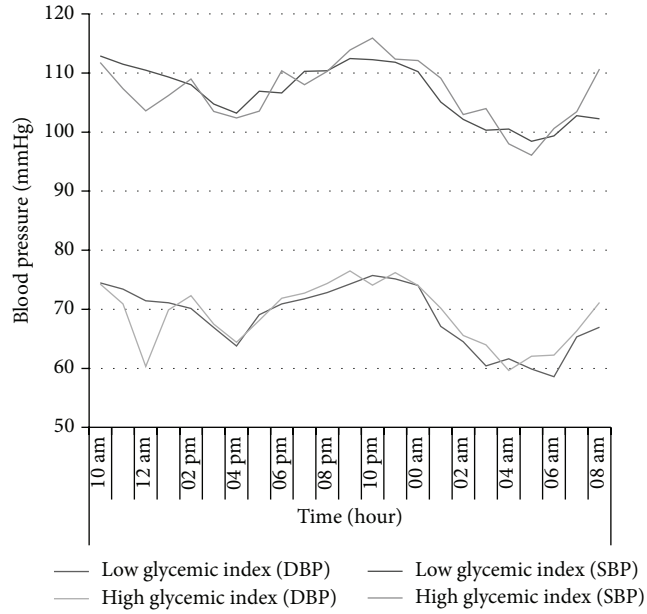

Figure 1: Constant SBP and DBP measurements in HGI and LGI groups at baseline and after the 24-hour interventions (values are expressed as mean ± SEM).

Data analysis showed that both dietary plans resulted in reduced SBP and DBP after the intervention, although only changes in the LGI period were significant ($P = 0.001$ and $P = 0.002$, resp.). In fact, in the HGI period, there was no significant change in SBP or DBP ($P = 0.6$ and $P = 0.06$, resp.) (Table 4).

After analysis divided by day and night (overnight rested and fasted) showed reduces in SBP and DBP over night were significant only in the LGI period ($P = 0.01$ and $P = 0.02$) (Table 5).

BP analysis showed no significant differences in the mean and changes of SBP or DBP between LGI and HGI period during 24 hours ($P = 0.89$ and $P = 0.31$, resp.) but since SBP and DBP were constantly evaluated during day and night, significant differences were observed between the two periods at night ($P = 0.01$ and $P = 0.04$) (Table 6). The area under the curve was 2344.4 for SBP and 1508.89 for DBP in the LGI period. Also, the area under the curve was 2344.03 for SBP and 1516.08 for DBP in the HGI period (Figure 1).

3.2. Heart Rate (HR). We analyzed the relationship between HR and changes in dietary GI and GL intakes.

There was a significant decrease in HR after the intervention in the two periods ($P = 0.02$ and $P = 0.01$, resp.) (Table 4). But after analysis divided by day and night (overnight rested and fasted) there was only significant reduce in HR in LGI period (Table 5).

However, the analysis of HR showed no significant difference in 24-hour mean and changes of HR between LGI and HGI periods ($P = 0.76$) (Table 6).

Table 4: The effects of LGI and HGI foods on SBP and DBP.

Characteristics	HGI diet			LGI diet		
	Baseline	At the end of the intervention	*P* value	Baseline	At the end of the intervention	*P* value
SBP (mmHg)	111.80 ± 9.57	110.66 ± 9.85	0.60	112.86 ± 9.33	102.26 ± 14.18	**0.001***
DBP (mmHg)	74.26 ± 10.09	71.16 ± 9.16	0.06	74.46 ± 7.61	66.96 ± 10.39	**0.002***
HR (bpm)	79.60 ± 12.77	71.13 ± 13.23	**0.01***	81.03 ± 12.71	72.23 ± 10.62	**0.02***

* $P \leq 0.05$; intragroup comparison of baseline and after intervention (after 24 hours). Results were performed by paired *t*-test for normally distributed data and by Wilcoxon test for nonnormally distributed data.

Table 5: The effects of LGI and HGI foods on SBP and DBP divided by day and night.

	Characteristics	HGI diet			LGI diet		
		Baseline	At the end	*P* value	Baseline	At the end	*P* value
Day (10 am to 9 pm)	SBP (mmHg)	111.80 ± 9.57	139.1 ± 10.64	0.26	112.86 ± 9.33	112.43 ± 9.83	0.79
	DBP (mmHg)	74.26 ± 10.09	76.50 ± 8.43	0.16	74.46 ± 7.61	74.30 ± 8.99	0.91
	HR (bpm)	79.60 ± 12.77	77.13 ± 10.13	0.28	81.03 ± 12.71	76.63 ± 11.69	**0.007***
Night (10 pm to 8 am)	SBP (mmHg)	115.9 ± 9.96	110.66 ± 9.85	0.1	112.27 ± 10.62	102.26 ± 14.18	**0.01***
	DBP (mmHg)	74.10 ± 9.80	71.16 ± 9.16	0.65	74.30 ± 8.99	66.96 ± 10.39	**0.02***
	HR (bpm)	75.40 ± 17.53	71.13 ± 13.23	0.23	81.06 ± 11.87	72.23 ± 10.62	**0.001***

* $P \leq 0.05$; intragroup comparison of baseline and after intervention (after 24 hours). Results were performed by paired *t*-test for normally distributed data and by Wilcoxon test for nonnormally distributed data.

Table 6: The comparison between percent changes of blood pressure in LGI foods and HGI foods.

	HGI diet	LGI diet	*P* value
Mean of 24-hour SBP (mmHg)	106.95 ± 6.34	106.39 ± 7.23	0.89
Mean of 24-hour DBP (mmHg)	69.50 ± 6.08	68.60 ± 5.8	0.31
Mean of 24-hour HR (bpm)	73.35 ± 8.72	74.03 ± 8.46	0.76
Changes in SBP after 24 hours (mmHg)	−1.13 ± 12.00	−10.60 ± 15.39	0.08
Changes in DBP after 24 hours (mmHg)	−3.10 ± 8.85	−7.50 ± 12.38	0.1
Changes in HR after 24 hours (bpm)	−8.40 ± 13.09	−8.8 ± 13.94	0.91
Changes in SBP during day (mmHg)	+2.10 ± 10.04	−4.33 ± 9.23	0.38
Changes in DBP during day (mmHg)	+2.23 ± 8.62	−0.16 ± 8.7	0.29
Changes in SBP during night (mmHg)	−3.23 ± 9.36	−10.16 ± 14.65	**0.01***
Changes in DBP during night (mmHg)	−2.93 ± 12.83	−8.76 ± 12.60	**0.04***
Changes in HR during day (bpm)	−2.46 ± 12.27	−4.40 ± 8.31	0.51
Changes in HR during night (bpm)	4.26 ± 19.17	8.83 ± 13.11	0.21

* $P \leq 0.05$; within-group comparison of baseline and 24-hour results by paired *t*-test for normally distributed data or by Wilcoxon test for nonnormally distributed data.

4. Discussion

In the present longitudinal study, we examined the effects of dietary GI and GL changes on BP and HR. This study demonstrated that LGI foods could significantly reduce SBP and DBP (102.26 ± 14.18 mmHg versus 112.86 ± 9.33 mmHg for SBP and 66.96 ± 10.39 mmHg versus 74.46 ± 7.61 mmHg for DBP) ($P = 0.00$ and $P = 0.002$, resp.). Also this study showed the night time BP was significantly lower in LGI period. This finding was in agreement with the results of a study by Philippou et al., who demonstrated that an LGI diet together with healthy eating and weight loss may be highly beneficial in reducing 24-hour BP [6]. Also, this finding was supported by previous studies, which demonstrated that LGI diets resulted in a significant reduction in SBP and DBP [8, 9].

Two interventional studies have demonstrated that lowering dietary GI decreases BP in adults [2, 10]. Furthermore, a previous systematic review and meta-analysis demonstrated that LGI diets can lower DBP in type 2 diabetic patients in the long run [11].

A reduction in postprandial plasma insulin may be of the mechanism which explains these changes. Insulin is known to activate the sympathetic nervous system and is a potential mediator of sodium retention and volume expansion, which result in higher BP [3].

We already demonstrated that increased dietary GI and GL lowered 24-hour SBP and DBP, although the difference was not statistically significant. These findings were supported by previous published data, showing that BP changes are insignificant after the HGI diet [6].

The results of the present study regarding the effect of HGI diet on BP were also confirmed by previous studies, which evaluated the effect of two hypocaloric LGI and HGI diets on obese children; the results demonstrated that both diets decreased BP in obese children [8, 9].

Conversely, a prospective study in 2004-2005 and 2009–2011, examining 858 students (aged 12 years), showed that increased intake of dietary CHO, specially HGI/HGL foods, could raise BP in females [3]; this finding was in contrast with the current results. However, it should be noted that this study had a large sample size, and participants were followed up for 5 years.

The current results showed a significant change in HR after the intervention in LGI and HGI groups during 24 hours. Also, Jenkins et al. demonstrated a significant difference in HR in their randomized controlled trial on 121 participants with type 2 diabetes mellitus after following both high wheat fiber and LGI diets [10].

To the best of our knowledge, this research is the first longitudinal study to examine the effect of dietary GI manipulation on 24-hour BP by adjusting the effects of confounding variables. Previous studies could not exclude confounding or unknown factors given the differences in subjects' characteristics such as age, weight, height, ethnicity, and BMI. Therefore, the possibility of selection bias, which limits the generalization of the results, could not be ruled out.

Also, in our study, the distribution of macronutrients and energy was similar in both diets. Power calculation using data from a study by Philippou et al. [6] and differences in SBP and DBP (differences of 3 and 13 mmHg) between the groups suggested a sample size of 30 subjects. It should be mentioned that the current study was performed over a short period of time; therefore, further longitudinal research is required for reaching a definite conclusion. Also, our study did not consider objective measurements such as biochemical factors and body composition.

5. Conclusion

In conclusion, the obtained results suggest that LGI foods may have significant reducing effects on SBP and DBP. Only the LGI group experienced a significant reduction in 24-hour BP, which may be related to the improvement in insulin sensitivity. However, other longitudinal studies with more comprehensive data are required to assess the relationship between BP, GI, and GL before reaching a definite conclusion.

Conflict of Interests

None of the authors have a personal or financial conflict of interests to disclose.

Authors' Contribution

All the authors read and approved the paper before submission.

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Research Article

Associations of Short Sleep and Shift Work Status with Hypertension among Black and White Americans

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Objective. The purpose of this study was to investigate whether short sleepers (<6 hrs) who worked the non-day-shift were at greater likelihood of reporting hypertension and if these associations varied by individuals' ethnicity. *Methods*. Analysis was based on the 2010 National Health Interview Survey (NHIS). A total of 59,199 American adults provided valid data for the present analyses (mean age = 46.2 ± 17.7 years; 51.5% were female). Respondents provided work schedule and estimated habitual sleep durations as well as self-report of chronic conditions. *Results*. Of the sample, 30.8% reported a diagnosis of hypertension, 79.1% reported daytime shift work, 11.0% reported rotating shift work, and 4.0% reported night shift work. Logistic regression analysis showed that shift work was significantly associated with hypertension among Blacks [OR = 1.35, CI: 1.06–1.72. $P < 0.05$], but not among Whites [OR = 1.01, CI: 0.85–1.20, NS]. Black shift workers sleeping less than 6 hours had significantly increased odds of reporting hypertension [OR = 1.81, CI: 1.29–2.54, $P < 0.01$], while their White counterparts did not [OR = 1.17, CI: 0.90–1.52, NS]. *Conclusions*. Findings suggest that Black Americans working the non-day-shift especially with short sleep duration have increased odds of reporting hypertension.

1. Introduction

Over the past thirty years, various hazards have been associated with working outside the conventional day shift, which is commonly referred to as shift work. Shift work has been linked to gastrointestinal disease [1], metabolic syndrome [2–4], cardiovascular disease [5–10], and cancer [11, 12]. Evidence shows that shift work has detrimental effects on mood, cognitive performance, and family life [13–15]. Additionally, recent studies suggest that circadian disruption caused by shift work may result in impaired glucose metabolism, type II diabetes, and hypertension [4, 16, 17].

Generally, shift workers are at greater risk for cardiovascular disease including obesity [18, 19], diabetes [4, 16, 20], hypertension [17, 21–25], and metabolic syndrome [2, 3, 26–29]. A 10-year follow-up study of Japanese factory workers found that those who were mainly shift workers had higher body mass index (BMI) and total cholesterol than their day shift counterparts [19]. In addition, individuals who switched from day to shift work had on average 1.03 kg/m^2 increased BMI [19]. A similar 14-year cohort study of Japanese male steel workers revealed that rotating shift work was an independent risk factor for increased systolic and diastolic blood pressure [25]. These results are consistent with a prospective cohort study of British workers who were studied over a period of 45 years [29]. Investigators demonstrated that males working the night/early morning shifts tended to have less favorable outcome for waist circumference, body mass index, triglycerides, HDL-C, and Hemoglobin A1C; however, systolic and diastolic blood pressure and total cholesterol were unaffected. By contrast, female workers mainly showed elevated triglyceride levels [29]. It is of interest to ascertain whether these associations are independent of the amount of habitual sleep duration, as shift work is known to result in shorter sleep duration (<6.5 hrs) [30], which is also linked to cardiovascular disease [31, 32].

Relatively little is known concerning ethnicity and its association with shift work and hypertension, an important cardiovascular disease. It is important to examine ethnic effects on such associations because of data suggesting that Black short sleepers may have an increased risk of hypertension [8]. Furthermore, data from the Nurses' Health Study II suggested that Black women on rotating shift schedules had a 46% increased risk of developing hypertension compared with their White counterparts [17]. The purpose of this study was to investigate whether short sleepers (<6 hrs) working the nonday shift were at greater risk of reporting hypertension. We also explored whether associations varied based on individuals' ethnicity.

2. Methods

2.1. Participants. A total of 59,199 Americans (age range: 18–85 years) who participated in the 2010 National Health Interview Survey (NHIS) provided sociodemographic and subjective data as well as data on self-reported chronic conditions for the present analysis. Analysis focused on associations among shift work, short sleep, and hypertension, while examining effects of ethnicity on these associations. Final weights provided by the CDC were applied to all analyses to adjust for the use of complex design in the NHIS. Of the sample, 82.8% were of White ethnicity and 17.2% were of Black ethnicity. Adults of both sexes were represented; 48.5% of the volunteers were men and 51.5% were women.

2.2. Procedures. NHIS is an ongoing, cross-sectional, in-person household interview survey conducted annually by the National Center for Health Statistics of the Centers for Disease Control and Prevention. The NHIS uses a multistage area probability design sampling noninstitutionalized representative of US civilian population. Probability samples of the adult population of all 50 states and the District of Columbia were obtained. The final sample was characterized by a response rate of 90%. Details on sample design can be found in Design and Estimation for the National Health Interview Survey [33].

During face-to-face interviews conducted by trained interviewers from the US Census Bureau, volunteers provided sociodemographic data and information about self-reported chronic conditions. The chronic conditions included hypertension and diabetes. Ethnicity was assessed by the standards recommended by Interagency Committee for the Review of the Racial and Ethnic Standards. Participants responded to the question "which one of these groups would you say BEST represents your race?"

Health risk data included smoking status and alcohol intake. Smoking status was defined as current, former, or never. Alcohol intake was assessed based on the responses to the following questions: "in your entire life, have you had at least 12 drinks of any type of alcoholic beverage?" Respondents who consumed <12 drinks in their entire life were classified as never-drinkers; those who consumed ≥12 drinks in any year or their entire life were classified as drinkers.

Self-reported diseases were defined based on affirmative responses to the following questions: "have you ever been told by a doctor or other health professional that you have [disease or condition]?" Thus, hypertension was defined by an affirmative response to the question: "have you ever been told by a doctor or other health professionals that you had hypertension?" Diabetes was defined by an affirmative response to the question: "other than during pregnancy, have you ever been told that you have diabetes?" Participants also estimated habitual sleep duration (using full hour units, i.e., 5 hours, 6 hours, and 7 hours); no information on specific sleep disorders was elicited during the interview. Habitual short sleep duration was coded as (<6 hours/night), which was referenced to 7-8 hours/night sleepers. Short sleep duration was defined as <6 hrs because this is consistent with a number of previous studies evaluating negative outcomes of short sleep [20, 31, 34–37]. Long sleep duration (>9 hrs) was not included in this study as it is less frequent than short sleep duration among shift workers [32, 35, 38]. Participants were also asked to rate their mood within the last 30 days prior to the interview. Using mood indices (e.g., feeling of sadness, hopelessness, worthlessness, and poor effort), a depression severity score was generated which was a composite score estimated using the K-6 scaling system [39]. Responses were used to generate a score ranging from 0 to 24. Scores ≥13 indicated a greater degree of emotional distress [40].

Surveys were conducted using computer-assisted personal interviewing (CAPI), which utilizes a computer program for data collection that guides the interviewer through the questionnaire. The interviewer enters survey responses directly into the computer. The program determines through a computer algorithm whether data entered by the user match against all possible responses to specific questions; the program also checks for consistency against other data collected during the interview and saves the responses into a survey data file [41].

2.3. Statistical Analysis. Since the NHIS dataset includes data from different samples using a multistage area probability sampling design, all analyses performed in this study were based on weighted statistics using the weights provided with the NHIS dataset. These final weights that accompany the dataset represent a product of weights for corresponding units computed in each of the sampling stages to account for variations in sampling strategies that might affect generalization of final results [41].

Frequency and measures of central tendency were used to describe the sample. In preliminary analyses, Pearson and Spearman correlations were used to explore relationships between variables of interest; only factors showing a P value <0.05 were considered in the final regression model [40]. ANOVA was used for group mean comparisons, and Chi square test was employed to assess differences in categorical variables.

Using multivariate-adjusted logistic regression analyses, we examined associations of shift work (evening, night, or rotating shift work schedules) and short sleep duration with hypertension stratified by ethnicity; stratified analysis was justified by preliminary analysis showing significant interaction between ethnicity and shift work status (Wald = 40.26; $P < 0.01$) and short sleep (Wald = 43.34; $P < 0.01$), even with adjustment for covariates. The first model assessed odds of

Table 1: Baseline data of participants in the 2010 National Health Interview Survey (NHIS).

Sociodemographic, health risk, and medical characteristics of NHIS participants						
Variable	Whites (SE)	95% (CI) lower	95% (CI) upper	Blacks (SE)	95% (CI) lower	95% (CI) upper
Age (mean)	46.9 (0.2)	46.6	47.4	43.2 (0.4)	42.5	43.9
Female gender (%)	51.0 (0.4)	50.2	51.9	54.8 (0.9)	53.1	56.6
Completed high school (%)	87.7 (0.3)	87.0	88.3	85.0 (0.6)	83.7	86.2
Income > 35 K (%)	68.0 (0.5)	66.9	69.0	50 (1.1)	47.8	52.3
Ever smoked 100 cigs in life (%)	43.0 (0.5)	42.1	43.9	34.4 (0.9)	32.6	36.2
Current drinker (%)	81.8 (0.4)	81.0	82.6	70.4 (0.9)	68.5	72.1
Emotional distress (%)	2.7 (0.1)	2.5	3.0	3.2 (0.3)	2.7	3.9
Diabetes (%)	9.9 (0.2)	9.4	10.4	13.2 (0.5)	12.2	14.2
Hypertension (%)	29.7 (0.4)	29.1	30.5	37.9 (1)	36.1	39.8

SE: standard error, CI: confidence interval.

Table 2: Distribution of work schedules among white and black NHIS participants.

Work schedules of white and black participants in the 2010 NHIS data						
Variable	Whites (SE)	95% (CI) lower	95% (CI) upper	Blacks (SE)	95% (CI) lower	95% (CI) upper
Regular daytime shift (%)	72.1 (0.5)	71.0	73.2	65.7 (1.2)	63.3	67.9
Regular evening shift (%)	4.9 (0.2)	4.5	5.5	8.0 (0.7)	6.7	9.6
Regular night shift (%)	3.2 (0.2)	2.9	3.6	5.9 (0.6)	4.8	7.1
Rotating shift (%)	9.5 (0.3)	8.8	10.2	13.2 (0.8)	11.7	14.8

SE: standard error, CI: confidence interval.

reporting hypertension among shift workers. The second model determined odds of reporting hypertension among shift workers who were also short sleepers. Covariates entered in the models were gender, age, income, education, tobacco use, alcohol use, emotional distress, and diabetes. BMI was not included as a covariate in the final models, as it was not statistically significant in preliminary univariate analyses. All analyses were performed using SPSS 20.0.

3. Results

Of the sample, 30.8% reported a diagnosis of hypertension, 79.1% reported daytime shift work, 5.9% reported evening shift, 11.0% reported rotating shift, and 4.0 % reported night shift work. Table 1 illustrates the demographic and comorbid characteristics of both White and Black participants. Blacks were more likely to report hypertension compared with their White counterparts (37.9% versus 29.7%). Table 2 illustrates the distribution of work schedules among White and Black participants. Of note, a higher percentage of Blacks worked the night shift (5.9% versus 3.2%) or rotating shift (13.2% versus 9.5%) schedules relative to their White counterparts.

In Table 3, logistic regression analysis shows that shift work was significantly associated with hypertension among Black shift workers, but not among White shift workers. Among White shift workers, age, tobacco use, and diabetes were significantly associated with increased odds of reporting hypertension. Among Black shift workers, male gender, age, alcohol use, and diabetes were associated with increased odds of reporting hypertension.

Table 4 shows results of logistic regression analysis of shift workers who were also classified as short sleepers (<6 hrs), referenced to those sleeping 7-8 hours. Analysis showed that Black shift workers classified as short sleepers had significantly increased odds of reporting hypertension. Analysis showed no significant increases in odds of reporting hypertension among White shift workers.

4. Discussion

The goal of this study was to evaluate whether shift workers who also experience short sleep duration are more likely to report hypertension among Black and White Americans. Our study showed that shift work was only significantly associated with increased odds of reporting hypertension among Black participants, but not among White shift workers. In addition, Black shift workers, reporting short sleep duration, had increased odds of reporting hypertension compared with Black shift workers with healthy sleep duration (7-8 hours). Of interest, these associations were not significant for White participants.

The lack of significant finding among White participants is inconsistent with previous findings especially in the context of European studies, which tend to show increased cardiovascular risk among White shift workers [3, 5, 6, 26, 29, 42–44]. We should note, however, that our findings are consistent with more recent studies regarding increased odds of hypertension among Black shift workers as opposed to White shift workers [17]. These discrepancies could not be explained by differences in sociodemographic and health risk characteristics on the basis of individuals' ethnicity. Logistic regression indicated that age, male gender, and diabetes were all

Table 3: Logistic regression analysis showing adjusted odds ratios (OR) and confidence intervals (CI) for hypertension among white (top pane) and black (bottom pane) shift workers.

Likelihood of reporting hypertension among white and black shift workers				
Variable	OR	95% CI lower	95% CI upper	*P*
White shift worker	1.01	0.85	1.20	0.88
Gender	0.83	0.75	0.93	<0.01
Age	1.06	1.06	1.07	<0.01
Income	0.97	0.84	1.12	0.65
Tobacco use	1.26	1.11	1.43	<0.01
Alcohol use	1.26	1.06	1.50	<0.01
Emotional distress	1.67	1.05	2.67	<0.05
Diabetes	3.74	3.10	4.52	<0.01
Variable	OR	95% CI Lower	95% CI Upper	*P*
Black shift worker	1.35	1.06	1.72	<0.05
Gender	1.23	0.97	1.56	0.09
Age	1.08	1.07	1.09	<0.01
Income	0.85	0.65	1.11	0.23
Tobacco use	1.24	0.96	1.60	0.10
Alcohol use	1.48	1.13	1.94	<0.01
Emotional distress	3.07	1.56	6.05	<0.01
Diabetes	6.28	3.99	9.88	<0.01

Table 4: Logistic regression analysis indicating adjusted odds ratios (OR) and confidence intervals (CI) for hypertension among white (top pane) and black (bottom pane) shift workers reporting short sleep duration.

Likelihood of reporting hypertension among white and black shift workers reporting short sleep				
Variable	OR	95% CI lower	95% CI upper	*P*
White shift worker with short sleep	1.17	0.90	1.52	0.23
Gender	0.79	0.69	0.91	<0.01
Age	1.06	1.06	1.07	<0.01
Income	0.93	0.77	1.11	0.41
Tobacco use	1.03	1.01	1.05	<0.01
Alcohol use	1.19	0.93	1.52	0.16
Emotional distress	1.52	0.87	2.67	0.14
Diabetes	3.58	2.74	4.67	<0.01
Variable	OR	95% CI lower	95% CI upper	*P*
Black shift worker with short sleep	1.81	1.29	2.54	<0.01
Gender	1.40	1.01	1.94	<0.05
Age	1.09	1.08	1.11	<0.01
Income	0.91	0.64	1.29	0.59
Tobacco use	1.26	0.91	1.75	0.17
Alcohol use	1.79	1.17	2.75	<0.01
Emotional distress	3.55	0.85	14.77	0.08
Diabetes	5.93	3.16	11.11	<0.01

significant contributors to increased odds of reporting hypertension among both White and Black participants. Tobacco use was a significant contributor to increased odds of hypertension in the White participants, and alcohol use was a significant contributor in Black participants. The fact that diabetes was the strongest predictor in our model accords with previous findings suggesting that nonconventional shift work increases the risk of hypertension and diabetes. Indeed, a recent laboratory study, which mimicked the conditions of shift work by combining sleep restriction and circadian rhythm disturbance, resulted in increased postprandial glucose and decreased resting metabolic rate [16]. These findings

are consistent with a study of nurses which found a dose dependent relationship between years working on rotating shift and risk of diabetes [4].

Our findings and previous literature suggest a relationship between shift work and short sleep duration with the presence of hypertension. Still a mechanism linking short sleep duration and shift work to hypertension is lacking. One hypothesis postulates that short sleep duration leads to sympathetic activation, which in turn results in high blood pressure [45, 46]. Other theories propose a disturbance in the circadian rhythm as the catalyst for a variety of pathways that lead to hypertension [23, 47–49]. One such study noted that people who work rotating or night shift work tended to display impaired blood pressure dipping at night after just one night shift [50]. Others propose that disturbances in circadian rhythm may lead to impaired endothelial function perhaps via decreased nitric oxide [50] and/or myocyte hypertrophy and fibrosis in animal studies [51]. In healthy men, cortisol secretion is inhibited during the first 4 hours of sleep [52]. A study of textile factory workers found that hair cortisol levels and BMI were increased in shift workers [53]. Disturbances in the circadian rhythm related transcription factor CLOCK affect acetylation of glucocorticoid receptors resulting in increased translation of glucocorticoid receptors and subsequent effects on end organ systems [48]. It is likely that the combination of sympathetic activation, endothelial dysfunction, and increased cortisol activity all contribute to the development of cardiovascular disease in shift workers especially those with short sleep duration.

Our study has notable limitations. First, we relied on subjective report of hypertension, especially diagnosis of hypertension in the past, which could not be verified with objective data. Secondly, we did not have data on subjective sleep disturbance or report of insomnia. Based on the Penn State cohort, those with insomnia and short sleep duration have a higher incidence of hypertension. Poor sleepers without insomnia had a marginal increased hypertension after adjusting for obesity [54]. Also in the Penn State cohort nonobese people, with subjective sleep disturbance, had an increased incidence of obesity [55]. Thirdly, night shift workers and rotating shift workers were categorized as a singular non-day-shift group. Previous work has shown that permanent night shift workers may be exposed to more sleep deprivation and may have different health behaviors like tobacco use, which would affect the risk of hypertension [56, 57]. Fourth, important information was unavailable such as presence of antihypertensive medications and diagnosis of sleep apnea. Additionally, we utilized cross-sectional data; thus, we could not ascertain long-term effects of shift work on hypertension or whether incidence of hypertension would be greater among shift workers. A previous cohort study of Belgian workers found an increased incidence of metabolic syndrome as well as a dose-dependent relationship [27]. Likewise, we could not establish the mechanism by which short sleep duration and shift work influenced hypertension.

Notwithstanding the limitations described above, our study has several strengths. First, we used a population-based representative sample of US adults, which enhanced generalizability of our findings. Many studies in the past have been conducted in relatively homogenous populations in Scandinavia [3, 58, 59] or Asia [22, 23, 25, 60]. Second, we investigated the association between ethnicity and short sleep and hypertension among shift workers, which heretofore has not been undertaken. Future studies should explore those associations among Hispanic and Asian populations as well. Investigations should also include large prospective cohort studies in the US utilizing diverse populations to provide information on incidence of hypertension in shift workers with short sleep duration.

5. Conclusion

Minimizing health risks among shift workers is a daunting challenge, a fact that has captured the attention of national organizations like the Center for Disease Control and Prevention. Our study suggests the need to explore modifiable factors that may compound detrimental effects of shift work and short sleep including alcohol consumption and tobacco use, which are established risk factors for cardiovascular disease among shift workers [42, 61, 62]. One promising intervention in this area is the implementation of workplace smoking cessation programs, which may reduce cardiovascular risk among shift workers. Another target of intervention may involve increased opportunity for healthy sleep duration by maintaining individuals on rotating shifts rather than on permanent night shift, which could mitigate risk of hypertension in shift workers [63, 64]. Improving availability of health food options in the workplace and providing opportunities for physical activity may also prove beneficial, as shift workers tend to eat more energy-dense foods and have less opportunity for physical activity [65]. In sum, a particular focus on reducing identified risk factors among Black short sleepers is of utmost importance since they are more vulnerable to the cardiovascular hazards of shift work.

Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

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Review Article

Sleep Deficiency and Deprivation Leading to Cardiovascular Disease

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Sleep plays a vital role in an individual's mental, emotional, and physiological well-being. Not only does sleep deficiency lead to neurological and psychological disorders, but also the literature has explored the adverse effects of sleep deficiency on the cardiovascular system. Decreased quantity and quality of sleep have been linked to cardiovascular disease (CVD) risk factors, such as hypertension, obesity, diabetes, and dyslipidemia. We explore the literature correlating primary sleep deficiency and deprivation as a cause for cardiovascular disease and cite endothelial dysfunction as a common underlying mechanism.

1. Introduction

Sleep is an essential part of human health and well-being. Sleep plays a vital role in an individual's mental, emotional, and physiological health. Not only does sleep deficiency lead to neurological and psychological disorders, but also vast amounts of literature have explored the adverse effects of sleep deficiency on the cardiovascular system. Decreased quantity and quality of sleep, whether due to sleep disorders or just through lack of proper sleep patterns, have been linked to cardiovascular disease (CVD) risk factors, such as hypertension, obesity, diabetes, and dyslipidemia [1–3]. Studies have shown that short durations of sleep are associated with greater risk of developing or dying from CVD [4]. While secondary causes of sleep deficiency leading to CVD have been well described such as obstructive sleep apnea, here we explore the literature correlating primary sleep deficiency and deprivation as a cause for cardiovascular disease through an underlying mechanism of endothelial dysfunction.

2. Sleep Deficiency and Deprivation: Defining the Problem

Sleep deprivation and deficiency have a high prevalence in western societies. The National Sleep Foundation reported that less than half (44%) of all Americans receive a good night's sleep almost every night [5]. According to the National Institute of Health, sleep deficiency is a broad concept that occurs (a) if an individual does not get enough sleep (sleep deprivation), (b) if an individual's sleeping habits are out of sync with the body's natural circadian rhythm (sleeping during the wrong time of the day), and (c) if the quality or quantity of sleep is diminished due to a sleep disorder or external factors [6]. Our review will focus on four specific variations of sleep deficiency: insomnia, acute total sleep deprivation (TSD), partial sleep deprivation (PSD), and night shift workers.

Acute TSD refers to the avoidance of sleep for a period of at least one night. PSD, or sleep restriction, refers to the reduction in the total sleep time relative to one's usual baseline during a 24-hour period. PSD is the most common form of sleep deprivation encountered in everyday life in modern societies [7]. Insomnia is defined as a predominant complaint of dissatisfaction with sleep quantity or quality, associated with one or more of the following symptoms: difficulty initiating sleep, difficulty maintaining sleep characterized by frequent awakenings or problems returning to sleep after awakenings, or early morning awakenings with

inability to return to sleep [8]. A shift worker is anyone who follows a work schedule that is outside the typical "9 to 5" business day. According to the Bureau of Labor Statistics, millions of Americans are considered shift workers, including doctors and nurses, pilots, bridge builders, police officers, customer service representatives, and commercial drivers. Such workers often do not sleep in sync with the circadian rhythm, are sleep deprived, and experience frequent sleep disturbances [9, 10].

3. Establishing the Link between Sleep Deficiency/Deprivation and Cardiovascular Disease

3.1. Endothelial Dysfunction. The endothelium is the thin layer of cells that covers the internal surface of blood vessels, cardiac valves, and several body cavities. These cells play a vital role in maintaining homeostasis by sensing changes in hemodynamic forces and blood-borne signals. In response to homeostatic changes, endothelial cells elicit relaxation and contractions of the underlying vascular smooth muscle cells releasing vasoactive substances. Among those substances, nitric oxide (NO) plays a key role [11].

When an imbalance of the actions of the endothelium toward reduced vasodilation and increased vasoconstriction as well as increased prothrombotic properties occurs, it is said that endothelial dysfunction is present. Arterial endothelial dysfunction is an important event central to the pathogenesis of atherosclerosis. Continued endothelial dysfunction contributes to plaque initiation and progression [12].

Endothelial function can be measured in coronary arteries and in the periphery by measuring vasomotor function after intra-arterial infusion of pharmacologic substances that enhance the release of endothelial NO. The disadvantage of these methods is their invasive nature, which generally makes them unsuitable for studies involving asymptomatic subjects. For this reason, noninvasive tests of endothelial function have been developed and are more commonly used. Flow mediated dilation (FMD) is an ultrasound-based method that measures arterial diameter in response to an increase in shear stress, which causes endothelium-dependent dilatation [13]. This method can be applied more widely for the evaluation of endothelial dysfunction and has been applied to patients with sleep disorders.

3.2. Insomnia. One major study, the HUNT 3 (Nord-Trøndelag Health Study) fitness study, has explored the connection between insomnia and endothelial function. The study produced negative results, providing no association between endothelial dysfunction and insomnia. There were no consistent associations between the cumulative number of insomnia symptoms and FMD. However, when the study analyzed individual insomnia symptoms, it found that certain symptoms might be related to endothelial dysfunction and, interestingly, those symptoms differed by gender. Among women, there was an inverse association of early awakenings with endothelial function, but there was an opposite association for men. In addition, women who reported daytime sleepiness had a higher FMD than other women [14].

The HUNT 3 study had followed earlier health studies in Norway including the HUNT study which researched the association between insomnia and ill health and showed that insomnia is a significant risk factor for myocardial infarction [15]. The negative results of the HUNT 3 fitness study were not expected. It should be noted that the study had several limitations that may have led to such results, such as a self-selection bias and the fact that the study restricted itself to individuals free of CVD and hypertension. This introduces a stratification bias excluding a significant population who may exhibit endothelial dysfunction.

3.3. Total Sleep Deprivation. In contrast to insomnia, there is more literature on the effects of TSD on endothelial function. One particular study which examined cardiologists on call for 24 hours showed that, after being on call, along with an increase in blood pressure (BP), thirteen out of the fifteen physicians had a brachial artery dilatation that did not reach 4.4%, and five of them did not have any dilation at all [16]. This analysis attributes the difference in endothelial function to stress since it is traditionally accepted that mental stress is linked to activation of the sympathetic nervous system. In this case apparently there was a double stress: stress induced by a lack of sleep and stress secondary to high level medical decision making. The differentiation between the results that were caused due to a lack of sleep and those due to the mental stress of being on call for a long period of time is not clear however. Ghiadoni et al. conducted a study investigating the link between mental stress and endothelial function and found that brief episodes of mental stress, like those encountered in everyday life, may cause transient (up to a period of 4 hours) endothelial dysfunction in healthy young individuals [17].

Another study by Sauvet et al., exploring the effect of acute sleep deprivation on vascular function in twelve healthy males, found that the endothelium-dependent and the endothelium-independent cutaneous vascular reactivity indices were significantly decreased after 29 hours of TSD. By contrast, heart rate, systolic blood pressure, and the normalized low-frequency component of heart rate variability (0.04–0.15 Hz), a marker of sympathetic activity, increased significantly within 32 hours of TSD [18]. This same group of researchers then conducted a follow-up study in rats. They found that TSD induced a reduction in endothelial-dependent vasodilation [19].

3.4. Partial Sleep Deprivation. The relationship between PSD and endothelial dysfunction has received more attention than TSD and insomnia. In the several studies performed in the literature, PSD has consistently been linked to decreased vasodilation. Covassin et al. conducted a study on 16 healthy subjects who underwent a 15-day inpatient protocol consisting of a three-day acclimation period, eight days of either sleep deprivation or normal sleep, and four days of recovery. Compared to the acclimation phase during which normal sleep occurred, FMD decreased during the experimental phase in the sleep deprived group ($8.6 \pm 4.6\%$ versus $5.2 \pm 3.4\%$, $P = 0.008$), while it remained unchanged in controls ($5.04 \pm 3\%$ versus $6.73 \pm 2.94\%$, $P = 0.109$) [20]. A study

conducted by Pugh et al. demonstrated that, compared to the control group who received three nights of full sleep and did not exhibit any changes in their endothelial function, the participants who received three nights of PSD (4 hours of sleep) had a decreased endothelial function by 46.7 ± 1.6% after the second night of sleep restriction but, interestingly, recovered after the third night of PSD [21]. Dettoni et al. observed the effects of PSD for five nights in 13 healthy males. They found a reduction in the maximum endothelial-dependent venodilation (100 ± 22 versus 41 ± 20%) [22].

3.5. Shift Work. Compared to the other sleep habits that were mentioned, shift work has received the most attention when considering its effects on endothelial function. One observational study conducted on 22 healthy female nurses showed that after they worked 3 sequential night shifts the FMD was significantly decreased from baseline FMD taken after one regular workday [23]. Suessenbacher et al. compared 48 male shift workers with 47 male nonshift workers from a glass manufacturer using the EndoPAT technique to determine peripheral arterial tone (PAT). They found that, despite a greater percentage of regular physical activity among the shift workers (16.7 versus 4.3%), shift work was associated with a reduced PAT index compared to working only on the day shift (PAT index 1.73 ± 0.4 versus 1.94 ± 0.5) [24]. While physical activity has been associated with better endothelial function [25], this study suggested that the effects of sleep deprivation override the benefits of physical activity on vascular health. Wehrens et al. studied the long term effects of shift work. Their study compared the difference in FMD after two groups (shift workers compared to nonshift workers) were put through sleep deprivation and recovery sleep in identical laboratory settings. After correcting for the difference in body mass index (BMI), there was a trend for lower %FMD ($P = 0.08$) observed among shift workers compared to nonshift workers [26]. Amir et al. conducted a study that had results consistent with this trend. Thirty healthy physicians who had worked night shifts for an average of 5 ± 3 years had their endothelial function examined after a regular workday as the baseline and after a continuous workday of 24 hours including a night shift. Overall, there was a significant decrease in FMD after shift work compared with baseline measurements (6.7 ± 4.8% versus 10.5 ± 4.5%). The authors more importantly also noted that FMD decreased significantly in all subsets except in physicians with a shorter (<3 years) history of night shifts. In these physicians with the shorter history, the change in FMD after the shift was independently related to the length of shift work history [27]. These results were consistent with those found in the previous study by Wehrens et al. Both articles suggested that there may be long term implications of shift work on vascular function.

4. Mechanisms of Endothelial Dysfunction Caused by Sleep Deprivation (Figure 1)

4.1. Sympathetic Activation. Sympathetic overactivity has been a proposed explanation to the link that is seen between sleep deprivation and endothelial dysfunction. Dettoni et al. attribute the decrease in the maximum endothelial-dependent venodilation found in healthy males after PSD to an increase in sympathetic activity as the participants also experienced an increase in percent low-frequency (50 ± 15 versus 59 ± 8) and a decrease in percent high-frequency (50 ± 10 versus 41 ± 8) components of heart rate variability, increase in low-frequency band of blood pressure variability, and an increase in their serum norepinephrine (119 ± 46 versus 162 ± 58 ng/mL) [22].

Other studies, however, have rejected the association of sleep deprivation and sympathetic activation. Of the nine studies that link sleep deficiency and endothelial function mentioned in our review, three studies had a significant change in blood pressure, four studies did not investigate blood pressure, and two studies saw no difference in blood pressure. Studies that did not show a change in blood pressure, or did show a change but the change came after evidence of endothelial dysfunction, argue that endothelial dysfunction may not be due to increased sympathetic activity of being awake for a prolonged period of time but rather due to another factor. In a study on rats by Sauvet et al., they concluded that while sleep deprivation did decrease endothelial vasodilation, it was not due to changes in blood pressure and was independent of sympathetic activity because it was still evident after pharmacological sympathectomy. Rather, it appears to be associated with NO synthase and cyclooxygenase pathway alterations, specifically, a decrease in the activity of those pathways [19]. The authors, however, mentioned that a persistent increase in sympathetic activity could lead to endothelial dysfunction. This was supported by studies that have shown that subjects with a greater history of night shift work are more likely to have more endothelial dysfunction than subjects who rarely took the night shift and therefore argue the direct causal effect of sympathetic activation [26, 27].

4.2. The Role of Nitric Oxide. Endothelial dysfunction is known to be related to the bioavailability of NO which can lead to disruption of vascular homeostasis. NO is responsible for the modulation of vascular dilator tone, regulation of local cell growth, and protection of blood vessels from injurious consequences of platelets and cells circulating in blood. NO therefore plays a crucial role in normal endothelial function [28]. In the study conducted by Suessenbacher et al. on female nurses, in addition to the fact that after working sequential night shifts endothelial function was impaired, the results also showed that mono-nitrogen oxides (NO_x) were also significantly decreased after 3 sequential night shifts compared with the baseline measurements (from 176.1 ± 65.1 mmol/dL to 131.8 ± 72.1 mmol/dL, $P = 0.033$), although, in the end, there was no correlation between changes in NO_x and FMD before and after 3 sequential night shifts ($r = -0.218$, $P = 0.356$) [24]. In rats, TSD was found to lead to a decrease in NO [29].

It is possible that the reduction in the bioavailability of NO in these sleep deprivation cases may be due to the decreased expression of NO synthase (eNOS) by endothelial cells or a lack of substrate or cofactors for eNOS activity [30, 31]. Altered signaling is also a possibility. However, when

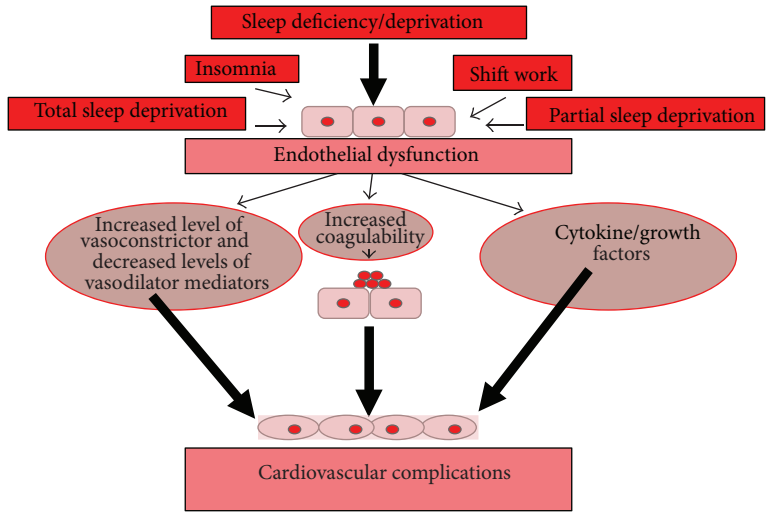

Figure 1

considering sleep deficiency, oxidative damage seems to be the mechanism. Oxidative stress occurs when there is an imbalance between oxidizing free radicals and antioxidant defenses. Free radicals or reactive oxygen species (ROS) such as O_2^- are quick to react with and inactivate NO. Thus, vascular oxidative stress can lead to a decrease in NO bioavailability. Under normal physiological conditions, endogenous antioxidant defenses minimize this interaction, thus allowing the body to maintain its ideal amount of NO. Sleep deprivation has been linked to increased uncompensated oxidative stress in peripheral tissues; however, a positive finding shows that recovery sleep can actually restore antioxidant activities [32]. A more recent study found that sleep deprivation does affect antioxidant activity by producing and imbalance in the oxidizing of the spleen cells. While the mechanisms of the cytoxic-like effects of sleep deprivation are likely "related to dysfunction in mitochondrial metabolism and vulnerability in cell signaling pathways," the exact mechanisms are not understood and require further study [33].

5. Conclusion

While there is evidence of an association between endothelial dysfunction and sleep deprivation, it still remains to be evaluated if sleep deprivation is a cause of or is associated with increased risk of CVD. However, endothelial dysfunction is an established independent risk factor for cardiovascular disease. Therefore, many of the factors that link endothelial dysfunction to cardiovascular disease are likely a result of the negative effects of sleep deficiency and deprivation. Further research in the area of sleep deprivation/deficiency is needed especially its relation to cardiovascular disease.

Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

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Research Article

Epidemiology of Hypertension Stages in Two Countries in Sub-Sahara Africa: Factors Associated with Hypertension Stages

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Studies using the revised hypertension classification are needed to better understand epidemiology of hypertension across full distribution. The sociodemographic, biological, and health behavior characteristics associated with different stages of hypertension in Ghana and South Africa (SA) were studied using global ageing and adult health (SAGE), WAVE 1 dataset. Blood pressure was assessed for a total of 7545 respondents, 2980 from SA and 4565 from Ghana. Hypertension was defined using JNC7 blood pressure classification considering previous diagnosis and treatment. Multivariate multinomial logistic regression analysis using Stata version 12 statistical software was done to identify independent predictors. The weighted prevalence of prehypertension and hypertension in Ghana was 30.7% and 42.4%, respectively, and that of SA was 29.4% and 46%, respectively, showing high burden. After adjusting for the independent variables, only age (OR = 1.32, 95% CI: 1.14–1.53), income (OR = 1.9, 95% CI: 1.04–3.47), and BMI (OR = 1.16, 95% CI: 1.1–1.22) remained independent predictors for stage 1 hypertension in Ghana, while, for SA, age (OR = 2.27, 95% CI: 1.53–3.36), sex (OR = 0.28, 95% CI: 0.08–1), and BMI (OR = 1.15, 95% CI: 1.07–1.25) were found to be independent predictors of stage 1 hypertension. Healthy lifestyle changes and policy measures are needed to promptly address these predictors.

1. Introduction

Worldwide prevalence estimates for hypertension may be as much as 1 billion individuals, and approximately 7.1 million deaths per year may be attributable to hypertension. The World Health Organization reports that suboptimal systolic blood pressure (SBP) >115 mmHg is responsible for 62 percent of cerebrovascular disease and 49 percent of ischemic heart disease (IHD), with little variation by sex [1]. Hypertension has been identified as the leading risk factor for developing congestive heart failure [2], stroke [3], chronic kidney disease, and end stage renal disease [4] and is ranked third as a cause of disability-adjusted life-years [5].

The risk of developing these complications depends on the level of elevated blood pressure and has been seen in all age groups starting from blood pressure as low as SBP 115 and DBP of 75 [6]. Data from observational studies involving more than 1 million individuals have also indicated that death from both IHD and stroke increases progressively and linearly from levels as low as 115 mmHg SBP and 75 mmHg DBP upward especially in individuals ranging from 40 to 89 years of age, indicating need for new blood pressure classification [6]. The risk of coronary heart disease increased significantly in the high range prehypertension individuals (SBP 130–139 or DBP 85–89 mmHg) but not in the low range prehypertensive population (SBP from 120 to 129 or DBP 80 to 84 mmHg) [7].

Because of the new data on lifetime risk of hypertension and the highly increased risk of cardiovascular morbidity associated with levels of BP previously considered to be normal, the JNC 7 report has introduced a new classification that includes the term "prehypertension" for those with BPs ranging from 120 to 139 mmHg systolic and/or 80 to 89 mmHg diastolic. This new designation is intended to identify those individuals in whom early intervention by adoption of healthy lifestyles could reduce BP, decrease the rate of progression of BP to hypertensive levels with age, or prevent hypertension entirely [8]. Robust population-based data using these recent blood pressure categories are still needed

to confirm prior estimates and inform policy decision makers in Sub-Saharan Africa.

Increasing urbanization has fueled social and economic changes in Sub-Saharan Africa, which have contributed to a surge in noncommunicable disease (NCD), including hypertension [9]. Epidemiological studies on hypertension in this region have been conducted over the years in an attempt to estimate the burden of hypertension, and these have reported variable rates within and between different population groups. In the first national Demographic and Health Survey, of 12,952 randomly selected South Africans aged 15 years, a high risk of hypertension was associated with less than tertiary education, older age groups, overweight and obese people, excess alcohol use, and a family history of stroke and hypertension [10]. Prehypertension was also more common in those aged 35 years compared with those aged <35 years and in overweight and obese people compared with people of normal weight [11]. Hypertension was defined in these studies as individuals with self-reported treated hypertension or with an average of 2 blood pressure measurements of at least 140/90 mmHg [9, 12, 13].

Prior studies on hypertension mainly focused on these dichotomous definitions of hypertension and did not examine the sociodemographic characteristics and risk factors for hypertension across full distribution of blood pressure. The current study follows the work of Basu and Millet on social epidemiology of hypertension in low- and middle-income countries from World Health Organization's Study on global AGEing and adult health (SAGE) [13]. Their work further showed additional variation in hypertension prevalence and social determinants of awareness when categorical definitions of hypertension were used compared to dichotomous definitions. Men had significantly lower probability of hypertension awareness than women at stage 1, but not at stage 2 [14]. This empirical study with an objective of studying social determinants and risk factors of different stages of hypertension tries to address this question. It determines the prevalence and independent predictors of different stages of hypertension in two countries in Sub-Saharan Africa, Ghana and South Africa.

2. Methods

2.1. Study Design and Population. We conducted a cross-sectional analysis of the Study on global AGEing and adult health (SAGE), WAVE 1 dataset which is a part of longitudinal survey program in WHO's multicountries study unit. The main SAGE surveys compile comparable longitudinal information on the health and well-being of adult populations and the ageing process from nationally representative samples in six middle- and low-income countries. We used the dataset of two Sub-Saharan countries, Ghana and South Africa. The SAGE study included nationally representative sample of persons aged 50 years and sample from younger adults aged 18–49 years as comparison which were also selected from both countries. Multistage cluster sampling was used [15]. The sampling design entailed two-stage probabilistic sample that yielded national and subnational estimates. In the first stage, a total sample of 600 enumeration areas (EA) in South Africa and 300 (EA) in Ghana were drawn from the master sample and used as the primary selection units (PSU). The second stage of the sample design was the selection of households from the EA's which formed the secondary sampling units. This stage of the process involved georeferenced aerial photograph maps of urbanized areas on which the locations of households were plotted. The total sample size of individuals was targeted to be 1000 people in the age group 18–49 years and 5000 people aged 50 years or older in each country.

2.2. Questionnaire. We recorded information about the household members from household and individual questionnaires; living place variable from the household questionnaire and sociodemographic characteristics, work history, blood pressure measurements, and risk factors including preventive health behaviors were taken from the individual questionnaire. Both the household and individual questionnaires were translated into six local South African and three local languages of Ghana. The respondents were interviewed face to face.

2.3. Blood Pressure Measurements and Classification. Blood pressure was measured three times while the respondent seated using automated OMRON R6 Wrist Blood Pressure Monitor, HEM-6000-E, Health Care Europe, B.V., Hoofddorp, The Netherlands. Such digital monitors have been shown to have high degree of agreement with mercury sphygmomanometers for systolic blood pressure [16, 17]. Average blood pressure was calculated arithmetically for the 3 measurements of each systolic and diastolic blood pressure. Missing values were excluded from being included in the study. Blood pressure classification was done using JNC 7 algorithm [1]. Prehypertension was defined as systolic blood pressure (SBP) measurement of 120–139 mmHg or diastolic blood pressure (DBP) of 80–89 mmHg. Stage 1 hypertension was defined as SBP of 140–159 mmHg or DBP of 90–99 mmHg and stage 2 as SBP of greater than or equal to 160 mmHg or DBP of greater than or equal to 100 mmHg. Accordingly normal pressure was defined as SBP of less than 120 mmHg and DBP of less than 80 mmHg.

All respondents were initially asked if they have ever been diagnosed with hypertension and if they did, whether or not they have been taking any kind of drugs or other treatment for the last 2 weeks and last 12 months. Normal blood pressure was defined as SBP <120 and DBP <80 mmHg and either no previous history of diagnosis or not taking antihypertensive medication. Those with SBP of 120 or more and DBP of 80 or more who did not have prior diagnosis nor treatment were designed as to have hypertension. They were subsequently stratified into three mutually exclusive different stages of hypertension. Those who reported as either having a diagnosis of hypertension previously or taking antihypertensive medication were excluded from analysis due to overlapping.

2.4. Sociodemographic Characteristics. All participants older than 18 years, of both sexes, were included in the study

and classified as living in urban or rural area. Current marital status (married or single that included unmarried, widowed, or separated) was asked about using the individual questionnaire. Educational level was assessed by first asking whether respondents have been in any school, and those who answered yes were asked for the highest educational level completed according to the international standard classification of education [18]. Respondents were asked whether they had ever worked for pay, type of work, and employer. Occupation responses were written verbatim by the interviewer, then coded, and mapped to the International Standard Classifications of Occupations (ISCO) scheme [19]. Classification of income quintiles was based on permanent income estimates derived from household assets and characteristics of the dwelling upon which The 2001 WHO World Health Survey/SAGE WAVE 0 relied [15]. Recent alcohol intake was asked for by asking whether the respondents have consumed alcohol in the past 30 days. Response was documented as yes and no. Current smoking (yes or no), with provision for the collection of information on other forms of smoking apart from cigarettes, such as cigars, pipes, snuff, or chewing smokeless tobacco, was asked about. Question was formulated based on guidelines for controlling and monitoring the tobacco epidemic [20]. Work related and sport or leisure time physical activities were separately asked in a typical week. Vigorous or moderate physical activities required hard or moderate physical effort and caused an increase in breathing or heart rate for at least 10 minutes [21]. Fruit and vegetable servings in typical 24 hours were asked about. Inadequate intake was defined based on WHO recommendations and labeled as less than 5 servings (80 g per serving) on a typical day [22].

2.5. Anthropometric Measurements. Height was measured in centimeters after the respondents took off their shoes, put their feet and heels close together, stood straight, and stood forward with their back, head, and heels touching the wall. Next body weight was measured in kilograms. Body composition and fatness were assessed using WHO body mass index (BMI) derived from measured weight in kilograms and normalized by dividing by height in meters squared. It was categorized as underweight <18.5, normal weight 18.5–24.9, overweight 25 to 29.9, and obese greater than or equal to 30. Since abdominal obesity is highly correlated with atherosclerotic cardiovascular morbidity and mortality than BMI indices [23], waist circumference was also used to measure central obesity. The interviewer identified the top of the hip bone and after making sure the tape measure is parallel to the floor all the way around the body measured waist circumference (WC). The National Cholesterol and Education Program: Adult Treatment Panel III (NCEP: ATP III) guideline was used to designate central obesity: accordingly men with WC measurements greater than or equal to 102 cm and women with greater than or equal to 88 cm were considered to have one [24].

2.6. Statistical Analysis. Stata version 12 statistical software was used to analyze data after being cleaned. The individual and household data were merged together. Living place variable was taken from the household data while all the others were included from the individual dataset. To make sure the results of the individual country dataset represent the respective country population, weighting at the country level was done which was available in the SAGE dataset. Individual weights were poststratified according to the 2009 projected population estimates in Ghana and to the 2009 medium midyear population estimates in South Africa [25]. Weighted estimates of different stages of hypertension prevalence were reported as proportions of the actual sample size. Invalid blood pressure measurements such as values of diastolic blood pressure greater than systolic and those in the outliers were considered missing and excluded from analysis.

The associations between sociodemographic, biological, and health behavior variables and stages of hypertension (prehypertension, stage 1, and stage 2) were assessed in a two-step procedure where individuals with the different stages of hypertension were compared separately with those having normal blood pressure. In the first step, each variable was evaluated independently in a bivariate multinomial logistic regression analysis with different stages of hypertension as dependent variable to generate unadjusted OR with respondents' characteristics in each country separately. Those variables with P values less than 0.2 were retained and entered into multinomial logistic regression model in ascending stepwise manner to determine variables that were independently associated with the stages of hypertension. A probability level of $P < 0.05$ was considered significant. Age and BMI variables were entered in the multivariable multinomial models as continuous due to fewer numbers of people in the most upper and lower categories. All other variables were retained as categorical.

2.7. Ethical Approval. Informed consent was obtained from each respondent for interviews and measurements of anthropometrics. SAGE study received ethical clearance from WHO ethical review committee [26].

3. Results

The total sample size of the study was 8939, 3974 from South Africa and 4965 from Ghana. Participants who have been diagnosed previously with high blood pressure or who were already taking treatment were excluded from analysis due to overlap and difficulty to stratify them into mutually exclusive hypertension stages. Those with previous diagnosis of hypertension were 587 (12%) in Ghana and 1,111 (28%) in South Africa. Individuals taking antihypertensive medications were 396 (8%) in Ghana and 981 (25%) in South Africa. Completed interview response in South Africa was 2853 (96%) and 5057 (99%) in Ghana. Of these blood pressure was assessed for a total of 7545, 2980 (75%) respondents from South Africa and 4565 (92%) from Ghana which was included for analysis (Table 1). A higher number of study participants in Ghana were males (50.2%) compared to 48.5% in South Africa. More people lived in Urban areas in South Africa (69.7%) compared to only 44.4% in Ghana. In South Africa,

Table 1: Sociodemographic, health behavior, and biological characteristics (%) of study subjects, by country and hypertension stages.

$N = 7545$	Ghana ($n = 4565$)					South Africa ($n = 2980$)				
	Normal	Pre-HTN	Stage 1 HTN	Stage 2 HTN	Total (%)	Normal	Pre-HTN	Stage 1 HTN	Stage 2 HTN	Total (%)
Sociodemographic variables										
Age groups (years)	**					**				
18–49	28.1	32.6	20.5	18.8	762 (76.9)	28.2	31.7	16.2	23.9	334 (79.7)
50–59	20.1	23.2	28.3	28.4	1532 (9.4)	9.1	20.9	24.9	45.1	1242 (11.1)
60–69	18.5	24.7	23.1	33.7	1055 (6.3)	6.9	20.6	28.5	44.1	803 (5.7)
70–74	18.4	26.7	23.9	30.9	837 (5.1)	9.5	15	33.1	42.4	424 (2.5)
80+	19.0	27.6	24.5	29	374 (2.3)	5.8	20.4	29.6	44.2	171 (1.1)
Sex						*				
Male	26.2	29.3	20.7	23.8	2466 (50.2)	16.4	33.9	18.5	31.2	1361 (48.5)
Female	25.9	32.1	22.6	19.4	2099 (49.8)	31.3	25.1	18.4	25.3	1617 (51.5)
Living place						*				
Urban	23.6	30.3	24	22.2	1747 (44.4)	28.3	28.6	18.3	24.9	1890 (69.7)
Rural	28	31.1	19.8	21.1	2818 (55.6)	14.7	31.4	18.2	35.7	1084 (30.3)
Marital status										
Married	25.6	28.1	23.8	22.5	1758 (26.6)	28.9	29.1	19.5	22.6	1346 (46.5)
Single	26.3	31.8	20.8	21.1	2782 (73.4)	20	29.4	17.8	32.8	1578 (53.6)
Educational level	*					**				
No school	21.9	27.6	22.1	28.4	2337 (31.1)	7.7	20.8	22.4	49.1	647 (7.3)
<6 yrs	29.3	30.3	23.5	17	498 (12.8)	5.5	23.4	22.2	48.9	556 (13.9)
Primary	26.4	29.3	24.8	19.6	567 (20.1)	10.4	28.9	22	38.7	557 (13.9)
Secondary	21.8	41.3	21	15.8	244 (10.9)	35.2	26.2	17.4	21.3	391 (27.7)
High school	29.5	32.3	18.2	20.1	737 (20.7)	40.3	19.2	18.4	22.1	221 (29.1)
University	36.8	28.8	18.2	16.3	154 (4.4)	41.7	27.1	11.6	19.6	143 (8.1)
Occupation	*									
Public sector	23.6	34.1	21.8	20.6	380 (7.2)	26.9	30.1	10.7	32.4	395 (19.8)
Private	26.7	20.1	24.1	29.1	180 (5.2)	13.4	32.7	23	31	1421 (53.1
Self-employed	25	32.3	22	20.7	3564 (80.8)	44	31.8	10.5	13.8	106 (4)
Informal	25.2	24.0	15	35.8	332 (6.8)	33.9	16.9	18.9	30.3	592 (23.1)
Income	**									
Quintile 1 (poorest)	33.4	28.3	21.5	16.9	939 (15.6)	20	30	21.2	28.8	640 (19.6)
Quintile 2	33	29	16.9	21.1	932 (18)	28.3	23.6	22.8	25.3	631 (20)
Quintile 3	19.3	31	20.8	28.8	922 (19.4)	27.4	19.6	17.3	35.6	545 (20.2)
Quintile 4	18.8	34.8	24.6	21.8	921 (22.2)	21.1	35.6	13	30.4	551 (19.5)
Quintile 5 (richest)	28.2	29.6	23.2	19.1	845 (24.9)	23.7	37.7	17.7	20.9	595 (20.8)
Biological variables										
BMI (kg/m^2)	**					**				
Underweight	31	33	14.4	21.5	670 (9.3)	21.1	35.7	8.2	35	130 (3.5)
Normal	30.6	29.4	19.8	20.2	2543 (54.4)	35.9	35.6	12.2	16.4	777 (36.1)
Overweight	21.4	32.8	22.2	23.6	889 (24.2)	32.4	21.2	21.4	25	849 (30)
Obese	10.8	30.4	33.4	25.3	444 (12.1)	5.7	23.2	25.7	45.4	1148 (30.5)
Waist circumference	*									
Normal	27.9	29.9	20.2	22	3608 (76.7)	24.5	32	18.4	25.1	1574 (63.2)
Abnormal	20.2	32.8	26.2	20.9	930 (23.3)	20	25.2	20.8	34	1180 (36.9)
Health related behaviors										
Smoking	*									
No	25.9	31.4	22.2	20.5	3416 (84.1)	26.5	32.3	16.9	24.4	1819 (67.6)

Table 1: Continued.

$N = 7545$	Ghana ($n = 4565$)					South Africa ($n = 2980$)				
	Normal	Pre-HTN	Stage 1 HTN	Stage 2 HTN	Total (%)	Normal	Pre-HTN	Stage 1 HTN	Stage 2 HTN	Total (%)
Yes	26.2	27.6	18.8	27.5	1143 (15.9)	19.1	23.2	22.2	35.6	1077 (32.4)
Current alcohol use										
No	25.9	31.7	20.7	21.7	1181 (44.3)	25.4	21.2	31.2	22.2	347 (33.5)
Yes	28.2	27.2	22.7	22	1492 (55.7)	14.9	27.8	18.5	38.8	489 (66.5)
Work related physical activity	*					*				
High	25.5	33.5	19.9	21.2	1868 (44.7)	30.7	15.6	27	26.7	306 (12.4)
Moderate	29	28.7	22.5	19.7	1400 (27.5)	33.3	28.1	14.5	24.1	852 (36.3)
Low	23.5	28.5	23.7	24.3	1289 (27.8)	16	33.6	19.3	31.1	1734 (51.4)
Fruit intake/day	*					**				
0-1	25.7	27.9	23.9	22.5	1726 (32.3)	17.6	24.9	21.1	36.4	1476 (46.3)
2–4	28	31.9	19.8	20.3	2374 (57.8)	29.8	34.2	17.4	18.6	1305 (50.2)
>=5	13.7	32.7	24.7	29	402 (9.9)	37.8	9.2	7	46	79 (3.5)
Vegetable intake/day	*					**				
0-1	29.9	24.1	24.5	21.5	1112 (24.9)	14.9	24.8	24.4	35.9	1160 (35.7)
2–4	24.1	32.4	21.2	22.3	3269 (74.3)	30.8	32.7	15.3	21.2	1592 (60.6)
>=5	21.8	36.2	29.8	12.2	57 (0.9)	5.4	10.1	21.7	62.9	116 (3.7)
Blood pressure number	957	1205	1108	1295	4565	301	647	738	1294	2980
Weighted prevalence (%)	26.1	30.7	21.6	21.6		24.1	29.4	18.5	28.1	

*$P < 0.2$, **$P < 0.05$.
n = number of observations in the sample.
All percentages (%) are put as weighted estimates of the sample to represent population.

the proportion of obesity was 30.5% as compared to 12.1% in Ghana. Income quintile distribution was similar in both countries. Only 26.1% of the respondents in Ghana and 24.1% in South Africa fulfilled the definition of normal blood pressure. Prehypertension was more prevalent in Ghana (30.7%) than South Africa (29.4%). The weighted prevalence of hypertension (both stages 1 and 2) was 42.4% in Ghana and 46% in South Africa. The age group distribution across stages of hypertension was similar in both countries, the majority of prehypertensive individuals being in the age group of 18 to 49. Obese individuals constituted 45.4% of stage 2 hypertension in South Africa while they constituted only 25.3% of stage 2 hypertension in Ghana.

Prehypertension was significantly associated in Ghana with income distribution (OR = 1.9, 95% CI: 1.11–3.23) and BMI category (OR = 2.64, 95% CI: 1.11–6.3) in the bivariate multinomial analysis when compared with normal blood pressure measurement while in South Africa age (OR = 2.66, 95% CI: 1.34–5.28) and educational level (OR = 0.18, 95% CI: 0.05–0.63) only had a significant association (Table 2). Income and BMI remained to have a significant association with stage 1 hypertension. In addition age emerged as a new variable with significant correlation with stage 1 hypertension in Ghana in the bivariate analysis (OR = 1.71, 95% CI: 1.25–2.33). In South Africa stage 1 hypertension was significantly associated with age of the study participants (OR = 6.02, 95% CI: 2.61–13.88), educational level (OR = 0.09, 95% CI: 0.02–0.49), type of occupation (OR = 4.32, 95% CI: 1.06–17.55), BMI category (OR = 11.72, 95% CI: 2.35–58.43), and number of vegetable servings per day in the bivariate multinomial analysis (OR = 0.3, 95% CI: 0.11–0.82). Age, income, and BMI remained to be significantly associated with stage 2 hypertension in the bivariate multinomial analysis in Ghana. In addition educational level (OR = 0.07, 95% CI: 0.02–0.35) became a significant correlate with stage 2 hypertension. In South Africa factors significantly associated with stage 2 hypertension were age, living place, educational level, and fruit and vegetable intake.

4. Multinomial Logistic Regression Model with Pooled Multivariable Analysis

4.1. Ghana. For the multinomial logistic regression analysis, 10 independent variables which were associated with hypertension stages at level of P value < 0.2 in the bivariate analysis were retained in the model. These were age, educational level, type of occupation, income quintile, smoking status, BMI category, abdominal waist circumference, work related physical activity, and fruit and vegetable intake per day. Those with P values <0.05 in the multivariable model were considered statistically significant and were considered independent predictors of hypertension stages (Figure 1). At prehypertension level BMI (OR = 1.08, 95% CI: 1.03–1.14), income (OR = 2,24, 95% CI: 1.27–3.97), and number of vegetable intakes per day were found to be independent predictors after being adjusted for the other variables in the model. Income and BMI remained independent predictors

Table 2: Association between sociodemographic, health behavior, and biological variables with stages of hypertension (pre-HTN, stage 1, and stage 2) compared to normal blood pressure: bivariate multinomial analysis.

$N = 7545$	Ghana ($n = 4565$)			South Africa ($n = 2980$)		
	Pre-HTN OR (95% CI)	Stage 1 OR (95% CI)	Stage 2 OR (95% CI)	Pre-HTN OR (95% CI)	Stage 1 OR (95% CI)	Stage 2 OR (95% CI)
Age groups (years)						
18–49	1	1	1	1	1	1
50–59	1 (0.78–1.29)	1.93 (1.47–2.54)*	2.12 (1.59–2.83)	2.06 (1.04–4.09)	4.77 (2.13–10.67)	5.88 (3.01–11.48)
60–69	1.15 (0.86–1.54)	1.71 (1.25–2.33)*	2.72 (2.02–3.67)	2.66 (1.34–5.28)	7.19 (3.38–15.28)	7.57 (3.87–14.82)
70–74	1.25 (0.94–1.66)	1.78 (1.26–2.51)*	2.51 (1.8–3.51)	1.4 (0.57–3.44)	6.02 (2.61–13.88*)	5.25 (2.39–11.5)*
80+	1.25 (0.8–1.97)	1.77 (1.1–2.84)*	2.29 (1.47–3.57)*	3.17 (1.19–8.43)*	8.95 (3.5–22.89)	9.09 (3.77–21.93)
Sex						
Male	1	1	1	1	1	1
Female	1.11 (0.78–0.58)	1.1 (0.75–1.61)	0.82 (0.56–1.21)	0.39 (0.14–1.09)	0.52 (0.19–0.44)	0.43 (0.17–1.06)
Living place						
Urban	1	1	1	1	1	1
Rural	0.86 (0.6–1.24)	0.69 (0.47–1.03)	0.8 (0.51–1.25)	2.12 (0.82–5.49)	1.92 (0.75–4.88)	2.76 (1.14–6.68)*
Marital status						
Married	1	1	1	1	1	1
Single	1.1 (0.71–1.72)	0.85 (0.55–1.3)	0.91 (0.59–1.4)	1.46 (0.49–4.34)	1.32 (0.46–3.77)	2.1 (0.8–5.52)
Educational level						
No school	1	1	1	1	1	1
<6 yrs	0.82 (0.45–1.49)	0.8 (0.44–1.44)	0.45 (0.25–0.8)	1.58 (0.38–6.53)	1.39 (0.44–4.34)	1.4 (0.47–4.15)
Primary	0.88 (0.52–1.49)	0.93 (0.53–1.64)	0.57 (0.33–0.98)*	1.03 (0.28–3.84)	0.73 (0.2–2.66)	0.58 (0.17–1.95)
Secondary	1.5 (0.77–2.9)	0.95 (0.48–1.92)	0.56 (0.26–1.2)	0.27 (0.07–1.05)	0.17 (0.05–0.61)	0.09 (0.03–0.3)
High school	0.87 (0.52–1.45)	0.61 (0.35–1.07)	0.53 (0.3–0.92)	0.18 (0.05–0.63)*	0.16 (0.04–0.7)	0.09 (0.02–0.33)
University	0.62 (0.25–1.56)	0.49 (0.18–1.34)	0.34 (0.11–1.06)	0.24 (0.05–1.13)	0.09 (0.02–0.49)*	0.07 (0.02–0.35)*
Occupation						
Public sector	1	1	1	1	1	1
Private	0.52 (0.17–1.57)	0.97 (0.29–3.23)	1.25 (0.38–4.09)	2.18 (0.4–12.03)	4.32 (1.06–17.55)*	1.93 (0.49–7.64)
Self-employed	0.89 (0.47–1.72)	0.95 (0.49–1.85)	0.95 (0.46–1.97)	0.65 (0.06–7.18)	0.6 (0.07–5.23))	0.26 (0.03–2.33)
Informal	0.66 (0.27–1.62)	0.64 (0.27–1.55)	1.63 (0.6–4.39)	0.45 (0.07–2.99)	1.4 (0.22–8.72)	0.74 (0.16–3.51)
Income						
Quintile 1 (poorest)	1	1	1	1	1	1
Quintile 2	1.04 (0.6–1.79)	0.79 (0.44–1.41)	1.26 (0.74–2.14)	0.56 (0.14–2.26)	0.76 (0.17–3.43)	0.62 (0.18–2.14)
Quintile 3	1.9 (1.11–3.23)*	1.67 (0.94–2.96)	2.95 (1.76–4.95)	0.48 (0.1–2.37)	0.6 (0.11–3.15)	0.9 (0.2–4.12)
Quintile 4	2.19 (1.3–3.68)	2.03 (1.14–3.64)*	2.29 (1.32–3.97)*	1.13 (0.28–4.6)	0.58 (0.15–2.29)	1 (0.27–3.73)
Quintile 5 (richest)	1.24 (0.72–2.12)	1.27 (0.74–2.21)	1.33 (0.73–2.42)	1.06 (0.25–4.43)	0.7 (0.2–2.42)	0.61 (0.18–2.06)
Biological variables						
BMI (kg/m^2)						
Underweight	1	1	1	1	1	1
Normal	0.9 (0.51–1.6)	1.39 (0.76–2.55)	0.95 (0.53–1.71)	0.59 (0.12–2.87)	0.88 (0.16–4.68)	0.27 (0.05–1.38)
Overweight	1.44 (0.76–2.74)	2.23 (1.09–4.56)*	1.58 (0.77–3.26)	0.39 (0.07–2.06)	1.71 (0.28–10.53)	0.47 (0.08–2.77)
Obese	2.64 (1.11–6.3)*	6.62 (2.79–15.69)	3.37 (1.37–8.26)*	2.42 (0.53–11.03)	11.72 (2.35–58.43)*	4.81 (0.98–23.54)
Waist circumference						
Normal	1	1	1	1	1	1
Abnormal	1.52 (0.97–2.38)	1.79 (1.12–2.87)*	1.31 (0.8–2.13)	0.96 (0.25–3.75)	1.38 (0.38–5.04)	1.66 (0.49–5.56)
Health related behaviors						
Smoking						
No	1	1	1	1	1	1
Yes	0.87 (0.56–1.34)	0.83 (0.51–1.36)	1.33 (0.85–2.07)	1 (0.33–3.04)	1.83 (0.57–5.84)	2.02 (0.69–5.95)

Table 2: Continued.

$N = 7545$	Ghana ($n = 4565$)			South Africa ($n = 2980$)		
	Pre-HTN OR (95% CI)	Stage 1 OR (95% CI)	Stage 2 OR (95% CI)	Pre-HTN OR (95% CI)	Stage 1 OR (95% CI)	Stage 2 OR (95% CI)
Current alcohol use						
No	1	1	1	1	1	1
Yes	1.27 (0.77–2.1)	0.99 (0.6–1.65)	1.08 (0.66–1.76)	0.44 (0.1–1.93)	0.98 (0.15–6.56)	0.33 (0.08–1.42)
Work related physical activity						
High	1	1	1	1	1	1
Moderate	0.75 (0.49–1.15)	1 (0.63–1.58)	0.82 (0.5–1.33)	1.66 (0.35–7.95)	0.5 (0.08–2.93)	0.83 (0.19–3.62)
Low	0.92 (0.57–1.5)	1.29 (0.75–2.23)	1.24 (0.72–2.16)	4.14 (0.9–19.13)	1.38 (0.26–7.42)	2.24 (0.56–8.98)
Fruit intake/day						
0-1	1	1	1	1	1	1
2–4	1.05 (0.72–1.53)	0.76 (0.5–1.16)	0.83 (0.55–1.25)	0.81 (0.28–2.32)	0.49 (0.17–1.38)	0.3 (0.11–0.81)*
>=5	2.2 (1.06–4.56)	1.94 (0.91–4.14)	2.42 (1.29–4.54)	0.17 (0.02–1.34)	0.15 (0.02–1.03)	0.59 (0.07–4.65)
Vegetable intake/day						
0-1	1	1	1	1	1	1
2–4	1.67 (1.09–2.57)	1.07 (0.69–1.68)	1.28 (0.78–2.12)	0.64 (0.24–1.68)	0.3 (0.11–0.82)*	0.29 (0.11–0.72)*
>=5	2.07 (0.58–7.43)	1.67 (0.36–7.63)	0.78 (0.22–2.7)	1.13 (0.19–6.74)	2.46 (0.29–20.65)	4.86 (0.66–35.82)

*$P < 0.05$.

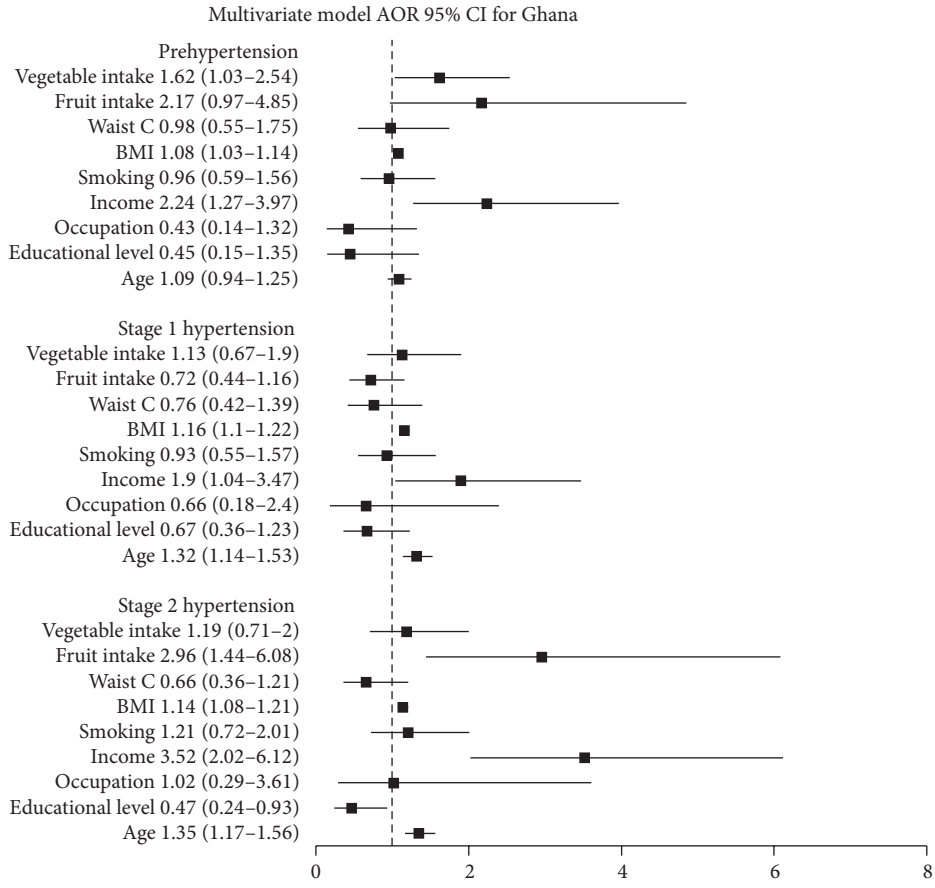

Figure 1: Adjusted odds ratios and 95% confidence intervals for stages of hypertension, Ghana.

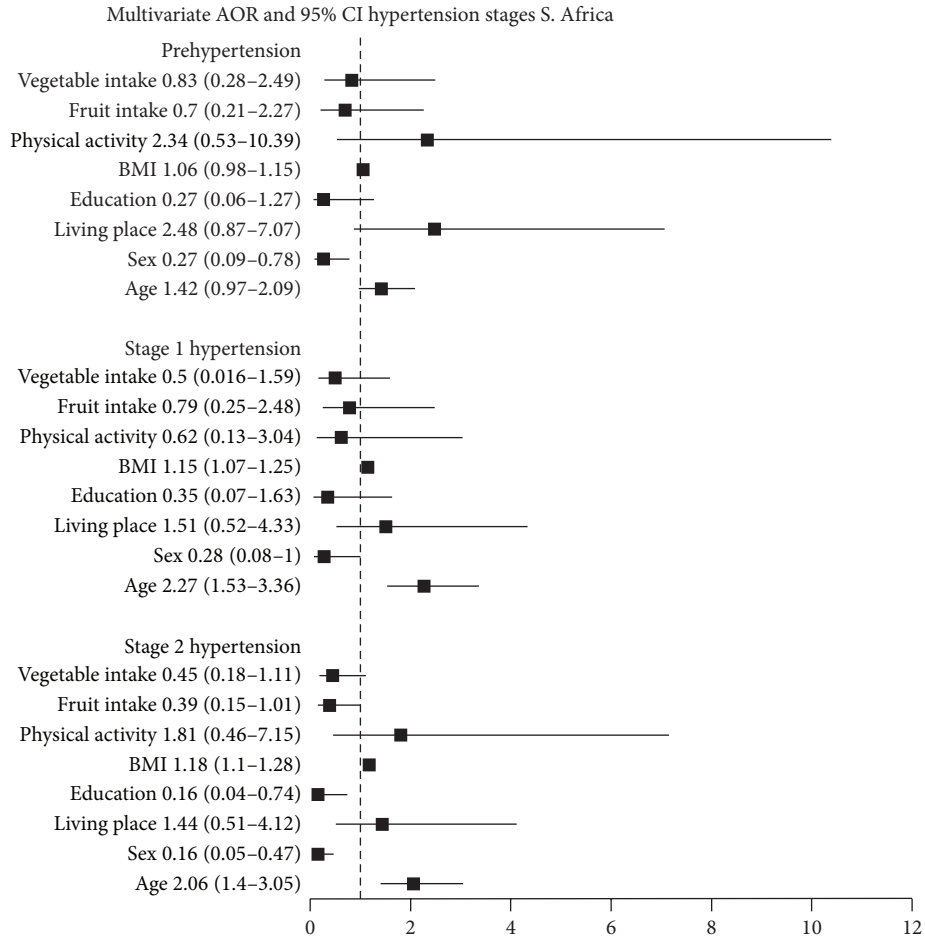

Figure 2: Adjusted odds ratios and 95% confidence intervals for stages of hypertension, South Africa.

for stage 1 hypertension as well. There was 32% increased risk of having stage 1 hypertension for every age increase by one year (OR = 1.32, 95% CI: 1.14–1.53). Age (OR = 1.35, 95% CI: 1.17–1.56), income (OR = 3.52, 95% CI: 2.02–6.12), and BMI (OR = 1.14, 95% CI: 1.08–1.21) remained as independent predictors for stage 2 hypertension as well. In addition higher educational level emerged as a protective variable against stage 2 hypertension in the model (OR = 0.47, 95% CI: 0.24–0.93).

4.2. South Africa. Eight variables which were associated with stages of hypertension in the bivariate analysis at probability level of $P < 0.2$ were retained in the multinomial logistic regression model. These were age, sex, living place, educational level, BMI category, work related physical activity, and fruit and vegetable servings per day (Figure 2). Only sex (OR = 0.27, 95% CI: 0.09–0.78) remained independent predictor of prehypertension in the multivariate logistic regression model after being adjusted for the other variables. Age and BMI emerged as independent predictors of stage 1 hypertension (OR = 2.27, 95% CI: 1.53–3.36 and OR = 1.15, 95% CI: 1.07–1.25). Sex remained as an independent predictor of stage 1 hypertension (OR = 0.28, 95% CI: 0.08–1). Being female resulted in 72% lower risk of having stage 1 hypertension than being male (OR = 0.28, 95% CI: 0.08–1). Age (OR = 2.06, 95% CI: 1.4–8.7), sex (OR = 0.16, 95% CI: 0.05–0.47), and BMI (OR = 1.18, 95% CI: 1.1–1.28) remained independent predictors of stage 2 hypertension in the final model. Educational level emerged as an independent predictor of stage 2 hypertension. Those with high school education tended to have 84% lower odds of stage 2 hypertension compared to those with no education (OR = 0.16, 95% CI: 0.04–0.74).

5. Discussion

The study has showed high burden of prehypertension and hypertension stages in the Sub-Saharan African countries, Ghana and South Africa. The weighted prevalence of hypertension (including both stages 1 and 2) was higher in South Africa (46%) compared to Ghana (42.4%). The high prevalence of hypertension in the current study is mostly due to higher age distribution of participants. More than 85% of respondents in Ghana and around 90% South Africans were in the age group more than 50, as part of the WHO SAGE study. The probability that a middle-aged or elderly individual will develop hypertension in his or her lifetime is 90% [27],

explaining the higher prevalence in this study. Higher prevalence of hypertension (77.3%) than the current study was also reported in hypertension and associated factors in older adults study in South Africa [28]. Comparing the two countries South Africa had higher prevalence of hypertension that could be explained by higher proportion of people living in urban area (69.7% in South Africa and 44.4% in Ghana) and increased number of obese people (30.5% in South Africa and 12.1% Ghana). In addition lower rate of physical activity and fruit intake per day was reported in South Africa.

The weighted prevalence of prehypertension was higher in Ghana (30.7%) than South Africa (29.4%). Higher reports were made from the PURE hypertension trial done on 153,996 adults aged 35 to 70 years, from 628 communities in 3 high-income, 10 upper-middle and low-middle-income, and 4 low-income countries of 36.8% [12]. These are groups of people with increased cardiovascular risk but who do not need pharmacologic treatment unless there is another compelling medical indication such as diabetes or chronic kidney disease [29]. They have higher likelihood of progression to overt hypertension and need lifestyle changes as a treatment such as weight reduction, physical activity, and decreased salt intake [30]. Progression from prehypertension to stage 1 hypertension was positively related to male gender, higher waist circumference, and having parents with hypertension in population-based study Keelung, Taiwan [31]. Identifying these individuals has high public health importance as such measures taken could delay or prevent progression or development of hypertension.

The weighted prevalence of stage 1 hypertension in Ghana was higher (21.6%) than in South Africa (18.5%) and the weighted estimate of stage 2 hypertension was higher in South Africa (28.1%) and Ghana (21.6%). Prior studies on these two countries were mainly done on dichotomized blood pressure classification using SBP of 140 mmHg or DBP of 90 mmHg and more. According to hypertension in South African adults, results from the Demographic and Health Survey, 1998, the prevalence rate of hypertension was 11% in males and 14% in females when blood pressure cut-off point (160/95 mmHg) was used [32]. In the current study BMI was an independent predictor for prehypertension in both Ghana and South Africa which was a similar finding in the study done in the Ashanti region of Ghana which showed age (OR = 1.56, 95% CI: 1.12–2.18; $P < 0.01$), obesity (OR = 2.71; 95% CI: 1.40–5.24; $P < 0.001$), and sex (OR = 2.36, 95% CI: 1.77–3.15; $P < 0.001$) being independent predictors of prehypertension on multivariable logistic regression [11]. In addition income became one of the strongest predictors for prehypertension in Ghana in our study, with higher income quintiles associated with higher levels of prehypertension. This was similar with household characteristics for older adults and study background from SAGE Ghana WAVE 1, which showed people with the higher income quintiles generally reported more hypertension (income quintile 5, wealthiest = 26.7%, versus quintile 1, poorest = 5.5%) and received more current and chronic therapy [15]. Other studies in US and Canada have shown the opposite effect; inverse linear relationship between household income and hypertension prevalence in the United States, but no evidence of such a relationship in Canada, was seen due to similar burden of hypertension across different socioeconomic classes [33]. Middle-income was a high correlate in another study in urban India [34]. Getting income data reliably was difficult as income was generated from ho usehold assets and converted later to quintiles, hence requiring cautious interpretation of result. The proportion of both overweight and obese was higher in the 4th and 5th income quintiles than the lower ones (23% and 30%, resp.) which could explain the high prevalence of prehypertension in the group.

Being in the higher BMI category contributed significantly to having prehypertension and could be related to the low physical activity of the current study participants [35]. Those with the lowest work related physical activity had the highest rates of prehypertension. South Africa has one of the lowest rates of insufficient physical activity (49% in adult women and 43% in adult men) compared to global figure of 17% and Africa's coverage of about 10% [36]. Some of the explanations were high rate of urbanization, increased mechanized labour, and television watching [37]. The very low report of physical activity contributing to both obesity and prehypertension needs to be addressed in South Africa by clinicians, public health specialists, patients, and policy makers at the government level.

We have tried to see the social determinant and risk factors for different hypertension stages (1 and 2) separately and whether they differ in the two countries and across different hypertension stages in the same country. The study has showed only age, income, and BMI remaining as independent predictors of stage 1 hypertension in Ghana. We found educational level and number of fruit intakes per day having an inverse relationship to stage 1 hypertension in South Africa in the bivariate multinomial analysis. This is similar with the first demographic and health survey study: determinants and treatment of hypertension in South Africa which showed higher risk of having hypertension with less than tertiary education [10]. Adults with no education or less than primary school were more than 50%, and the highest report of stage 1 hypertension was seen in this group in the current study. Curriculum reforms and models to increase opportunity of education in the postapartheid education system are undergoing [38] and should be further strengthened.

Increasing fruit and vegetable intake was seen to have significant blood pressure lowering effect in stage 1 and stage 2 hypertension. This effect was not seen in the final model. The finding is consistent with other trials that demonstrated the greatest benefit of dietary changes at lower stages of hypertension [30]. The DASH (Dietary Approaches to Stop Hypertension) trials introduced the DASH diet which is comprised of four-five servings of fruit, four-five servings of vegetables, two-three servings of low-fat dairy per day, and <25 percent fat [39]. Drop in average systolic blood pressure by 11.4 mmHg and diastolic blood pressure by 5.5 mmHg in hypertensive individuals has been seen as early as two weeks, with the DASH diet. Increasing fruit intake is thus highly recommended in individuals especially with lower stages of hypertension to prevent progression of disease. Countries should be working on ways to make availability of fruits accessible and affordable. The weighted estimate of people

taking the recommended fruit intake was very low (9.9%) in Ghana and (3.5%) South Africa. Vegetable intake was even much worse (0.9%) in Ghana and (3.5%) in South Africa. The wide confidence interval and attenuated beneficial effects of fruits and vegetables could be attributed to the very little proportion of people in these categories making the expected statistical association loose.

Though smoking cigarette was one of the most important risk factors for cardiovascular disorders and acute myocardial infarction in the INTERHEART Africa study [40], it was associated only in the bivariate analysis when studied individually. The effect was lost when multiple variables were retained in the regression model in both countries at every stage of hypertension. The incidence of hypertension increases in those who smoke 15 or more cigarettes per day [41] and could be the reason why strong association was not seen as only less than 2% individuals (Ghana) and around 7% (South Africa) smoked more than 15 cigarettes per day. Other studies have also documented "lower blood pressure measurements in those habitual smokers than nonsmokers due to weight loss and some vasodilatory effect of cotinine a metabolite of nicotine" [42, 43].

Only increasing age, income, BMI, and educational level were found to be independent risk factors for stage 2 hypertension in the final model in Ghana. There was no significant variation of stage 2 hypertension between sexes in Ghana, although it is known that men had higher systolic blood pressure measurements in early adulthood, while older women have steeper age-related rate of rise [27]. This could be in part due to the higher proportion of women who are overweight and obese in both countries.

This particular study has assessed the burden of hypertension in Sub-Saharan African countries. It focused mainly on risk factors and social determinants across different stages of hypertension among the two countries. This helps to identify newly emerging associated risk factors at different stages of hypertension and helps to be able to recommend measures accordingly. As it is always said "Prevention is better than Cure," we also recommend identifying individuals and treating accordingly at pre- and early hypertension stages, where the maximum benefit of lifestyle changes can be seen. These include having regular and intense physical exercise, reduction of body weight which can decrease average SBP by 5–20 mmHg for every 10 kg weight loss [1], increasing the opportunity to have basic education for all, and educating people with higher income in Ghana who are at high risk of prehypertension and subsequent overt hypertension due to probable acculturation to change their lifestyle. Government bodies at policy level and health specialists need to design methods to improve diagnosis and treatment of hypertension at earlier stages in respective countries.

6. Limitation

One of the major limitations of the current study was high number of missing and some invalid values in the original dataset. Missing and invalid blood pressure measurements accounted for 8% in Ghana and 25% in South Africa. They were excluded during the data cleaning period and not included in analysis. Alcohol consumption was an independent variable with the highest missing values (63%) in Ghana and (35%) in South Africa. This could be the reason for not seeing the expected protection from moderate dose of alcohol against hypertension and increased risk from excess dose [44]. The other components of therapeutic lifestyle changes that include intake of salt, saturated fat, and amount of calories [45] were not included in the SAGE questionnaire and their association with hypertension was not studied. The current study as any other cross-sectional studies determines only associations that are statistically significant without inferring causality. Further cohort studies that examine risk and causality are recommended. And finally using the JNC 7 blood pressure classification that was originally designed for US population and using its blood pressure cut-off points for Sub-Saharan population could impose risk of overgeneralization. Blood pressure cut-off points at which cardiovascular morbidity starts should be looked for in Sub-Saharan Africa context and guidelines should develop in the future.

Abbreviations

AOR: Adjusted odds ratio
BP: Blood pressure
BMI: Body mass index
CVD: Cardiovascular disorder
CI: Confidence interval
DASH: Dietary approaches to stop hypertension
DBP: Diastolic blood pressure
EA: Enumeration area
HTN: Hypertension
IHD: Ischemic heart disease
ISCO: International standard classification of occupation
JNC 7: Joint national committee 7 for hypertension
NCD: Noncommunicable disease
NCEP: ATP III: National Cholesterol Education Program: Adult Treatment Panel III
OR: Odds ratio
PSU: Primary selection unit
SA: South Africa
SAGE: Study on global AGEing and adult health
SBP: Systolic blood pressure
WC: Waist circumference
WHO: World Health Organization.

Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

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Review Article

Implications of Renal Denervation Therapy in Patients with Sleep Apnea

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Obstructive sleep apnea (OSA) syndrome is a prevalent condition characterized by repeated episodes of obstruction of the upper airway, leading to intermittent hypoxemia and important endothelial and anatomical dysfunctions that cause cardiovascular and cerebrovascular disease. The finding of the relationship between OSA and hypertension, especially resistant hypertension (RHT), has increased the interest in therapeutic strategies that affect renal sympathetic activity in these patients. The observational studies published until now demonstrated that renal denervation therapy can reduce the severity of OSA syndrome. Renal sympathetic denervation (RDN) could be a future therapeutic possibility for conditions other than RHT, such as atrial fibrillation, heart failure, obesity, and OSA syndrome, where renal sympathetic system plays an important physiological role. The aim of this review was to elucidate the implications of renal sympathetic activity in OSA syndrome.

1. Introduction

The apnea-hypopnea sleep (AHS) syndrome was firstly described in 1976 by Guilleminault et al. [1]. It affects 3–7% of the general population and is characterized by repeated episodes of obstruction of the upper airway during sleep.

The apnea-hypopnea index (AHI) is used to measure the severity of obstructive apnea. Diagnosis is defined as an AHI > 5 accompanied by disease-related symptoms [2].

OSA syndrome and its relationship with HT have been well established [3]. An increase in the AHI implies an increased risk of developing HT [4]. The factors involved in this cardiovascular issue are endothelial dysfunction and systemic inflammation, which lead to activation of the sympathetic tone. Excess sympathetic tone plays a decisive role in the development of RHT [5]. It is an independent risk factor for cardiovascular risk, which is responsible for ischemic heart disease, atrial fibrillation, heart failure, stroke, and sudden death [6]. Two-thirds of the patients with acute ischemic stroke develop OSA syndrome. The presence of OSA syndrome in patients who suffered from cerebrovascular events determines impairment of cognitive function during the acute and subacute phases of stroke [7].

HT is a major public health issue worldwide, not only because of its high prevalence (30–45% of the general population, reaching 60% in the elderly), but also because of the impact on cardiovascular morbidity and mortality. Population studies have reported that one-third of the hypertensive patients develop apnea-hypopnea sleep (AHS) syndrome and that 40% of patients with AHS syndrome are hypertensive [4, 8].

It has been observed that OSA syndrome is present in 75% of patients diagnosed with RHT; nevertheless, its prevalence is much lower (38%) in hypertensive patients with controlled blood pressure (BP) [9]. Cardiovascular risk was found to be significantly higher in patients with RHT than in those without RHT [10]; this association opens the possibility that OSA syndrome and HT share similar physiopathological mechanisms contributing to both pathological processes. Recent expert information recommends the treatment of

OSA syndrome as part of the management of patients with RHT [11–13].

The increase of sympathetic activity is involved in the development, management, and the evolution of the hypertensive state of patients with OSA syndrome. It implies that sympathetic deactivation can be seen as a goal of treatment. Small observational studies published so far reported that RDN can decrease the severity of OSA syndrome. RDN therapy is having an important role in the treatment of other diseases apart from HT; in fact, beneficial effects of RDN therapy in diseases other than HT where the renal sympathetic system plays an important role have been reported, such as atrial fibrillation, heart failure, obesity, or diabetes. The aim of this review was to elucidate the implication of renal sympathetic activity on the OSA syndrome.

2. Physiopathological Factors of OSA Syndrome

Many physiopathological factors have been described involved in the development of AHS syndrome. Some of the factors that promote the collapse of the upper airway are the narrowing of this airway, excessive loss of muscle tone, and defective upper airway protective reflexes mediated by overstimulation of sympathetic nervous system [14–16].

The neurophysiological factors involved in the development of HT in patients with AHS syndrome are interacting with each other [17]. Increased sympathetic tone implies the following physiological changes (Figure 1):

(1) Intermittent hypoxia due to apnea and hypopnea triggers an excess of sympathetic activity by the activation of the carotid chemoreceptors; it leads to direct vasoconstriction and the subsequent stimulation of the renin-angiotensin-aldosterone system (RAAS) as well as increased levels of endothelin and angiotensin II. Activation of the renin-angiotensin axis produces fluid retention due to sodium reabsorption; it seems to lead to edema in the peripharyngeal walls, which predisposes to upper airway obstruction [18, 19].

(2) The increase in the sympathetic tone in patients with OSA syndrome produces renal activation of the autonomic nervous system. The kidneys are connected to the brain by afferent and efferent pathways. Hyperactivity of the autonomic nervous system stimulates renin release from the juxtaglomerular apparatus, then activating β1 adrenoreceptors; this increases the circulating volume when sodium retention increases, and renal blood flow decreases through the α1 adrenoreceptors.

Renal afferent activation determines an increase of the sympathetic activity in the central nervous system (CNS), involving the vascular system, heart, and the other peripheral organs, leading to HT and its degree of severity [20].

(3) Sympathetic hyperactivity reduces the dilating effect of the upper airway muscles mediated by the genioglossal nerve and predisposes to pharyngeal obstruction [21]. Excess of sympathetic tone increases pharyngeal wall thickness and favors peripharyngeal fluid accumulation promoting the development of OSA syndrome, with recurrent episodes of hypoxia, sleep fragmentation, and the subsequent increase of the sympathetic tone [22].

(4) The physiological stimuli associated with apnea produce the formation of endogenous vasoactive substances and decrease the levels of nitric oxide, a potent vasodilator. It has been demonstrated that the use of CPAP during the night increases the circulatory levels of nitric oxide. Ischemic and reperfusion events associated with apnea lead to endothelial injury [23].

3. Results of the Major Clinical Studies in Patients with OSA Syndrome Undergoing Renal Sympathetic Denervation

Symplicity HTN-1, HTN-2, and HTN-3 trials are the most relevant studies concerning the clinical use of RDN therapy [30–32]. The initial studies demonstrated a significant decrease of BP levels at 3 years in patients with RHT.

Nevertheless, the Symplicity HTN-3 study which enrolled 535 randomized patients with a 6-month follow-up was not able to confirm the results previously obtained. There was no significant between-group difference in the change in office blood pressure at 6 months. This finding has questioned its efficacy. However, the responses with regard to systolic and diastolic blood pressure were significantly greater in the denervation group than in the sham-procedure group. It seems to be demonstrated that RDN therapy reduces renal sympathetic secretion and leads to a systemic decrease in sympathetic tone.

Some small studies have demonstrated a significant decrease of AHI in patients with OSA syndrome after undergoing RDN; this can explain the relationship between HT, OSA syndrome, and excess sympathetic tone. RDN has the potential effect of decreasing sympathetic overactivity in patients with OSA syndrome [33].

The first studies demonstrating this relationship were carried out in animal models. RDN decreased BP rises and the incidence of secondary arrhythmias, during postapneic periods in OSA syndrome models. This decreased the susceptibility of these animal models to develop atrial fibrillation [34]. Furthermore, these effects seemed to be independent of the decreases found in BP levels, which gave more relevance to the role of the central sympathetic secretion.

A recent meta-analysis published by Shantha and Pancholy [24] included 5 relevant clinical studies [25–29] in humans (Table 1) with a total of 49 patients studied.

Three of these studies were carried out in Europe, where the RDN technique is more accepted. Of the five studies, that of Witkowski et al. evaluated specifically the role of RDN in the AHI, BP, and glycemic control. Although the number of patients involved in the study was small ($n = 10$), it showed relevant results. AHI was measured in the 10 patients by polysomnography, before and 6 months after undergoing RDN. The authors reported a decrease in the severity of

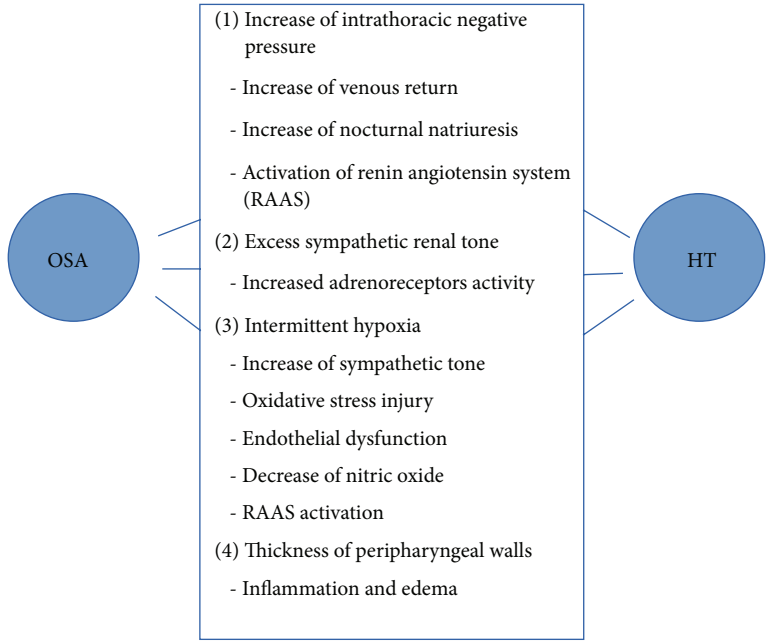

Figure 1: Relationship between OSA syndrome and arterial hypertension (HT).

Table 1: Major clinical studies carried out in patients with AHS syndrome undergoing RND therapy. Modified by Shantha and Pancholy [24].

Author	Year	Patients (*n*)	OSA patients	AHI pre-RDN	AHI post-RDN (6 months)
Damascelli et al. [25]	2013	24 RHT patients	2	63.3	26.5
Schmiedel et al. [26]	2013	40 RHT patients	16	25	17
Thakur et al. [27]	2013	21 RHT patients	6	21.1	10.5
Witkowski et al. [28]	2011	10 RHT patients, all with OSA	10 10	30.7	16.1
Zhao et al. [29]	2013	31 RHT patients	15	32	27

Resistant hypertension = RHT; obstructive sleep apnea = OSA; apnea-hypopnea index = AHI; renal sympathetic denervation = RDN; apnea-hypopnea sleep syndrome = AHS.

OSA syndrome in the patients after RDN, although without statistical significance due to the small size of the sample. The authors also reported that RDN therapy significantly decreased BP levels and improved the glycemic control of patients [28].

Zhao et al. [29] compared the response a total of 31 patients with OSA syndrome, 16 of them undergoing CPAP treatment and the other 15 treated with RDN.

The authors concluded that both CPAP and RDN treatments decreased OSA severity in the patients. They reported that the efficacy of CPAP treatment was higher in patients undergoing this therapy, since 6 months after treatments the AHI was lower in the patients treated with CPAP than in those who underwent RDN.

All 5 studies of the meta-analysis showed significant changes in BP after RDN, with a 6-month follow-up. The decrease in SBP was greater than in DBP. Furthermore, there were some evidences that the decrease was independent of the improvement in the severity of OSA found in the patients. The meta-analysis included 49 patients followed up during 6 months. The AHI was measured in all of them before and after RDN. The results demonstrated a reduction in AHI 6 months after RDN, as well as less nocturnal awakenings and improvement of nocturnal oxygen saturation.

4. Treatment of Sleep Apnea in Patients with Hypertension

Continuous positive airway pressure (CPAP), described by Sullivan et al. in 1981, is the treatment of choice for sleep apnea in hypertensive patients [35]. It improves the apnea episodes and prevents oxygen desaturation and the arousals (electroencephalographic awakenings), which results in a reduction in the morbidity and mortality of these patients [36].

Montesi et al. [37] carried out a systematic review and meta-analysis in 2012, which included 32 studies and a total of 2303 patients. The use of CPAP therapy was associated with a significant decrease in SBP, DBP, and mean BP values. BP decreases were mainly found in patients with higher daytime sleepiness, more severe OSA, and more compliance to CPAP therapy.

The mechanisms of the association between BP and daytime sleepiness could be related to the arousals, which occur at the end of the respiratory events, coinciding with repeated BP surges. Intermittent ischemic episodes increase BP by the activation of type I angiotensin II receptor. It seems that overactivation of the renin-angiotensin axis occurs independently of other factors [38]. RDN could have an important role in patients with higher sympathetic stimulation.

Although the hypotensive effect of CPAP seems to be moderate, decreases of 5 mm Hg in DBP reduce the risk of cerebrovascular accidents by 42% and all cardiovascular events by 31% [39].

Significant decrease of BP only 3 weeks after onset of CPAP treatment reinforces the importance of studying and treating OSA syndrome in patients with RHT.

5. Conclusions

CPAP is the treatment of choice in the management of patients with OSA; its use in the treatment of RHT is becoming increasingly more widespread. The important implications of morbidity in OSA syndrome make it necessary to seek new therapies that intervene in the physiological mechanisms related to cardiovascular events in these patients. Nowadays, it has been demonstrated that RDN improves the severity of OSA syndrome in patients with RHT. In this respect, RDN treatment could be considered in patients with excess sympathetic tone. Nevertheless, further clinical trial should be required before renal denervation can be applied to the study of OSA and other conditions such as obesity hypertension.

Disclosure

The authors agree with all criteria of publication of this journal.

Conflict of Interests

The authors declare no conflict of interests.

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Research Article

Hypertension Subtypes among Hypertensive Patients in Ibadan

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Background. Certain hypertension subtypes have been shown to increase the risk for cardiovascular morbidity and mortality and may be related to specific underlying genetic determinants. Inappropriate characterization of subtypes of hypertension makes efforts at elucidating the genetic contributions to the etiology of hypertension largely vapid. We report the hypertension subtypes among patients with hypertension from South-Western Nigeria. *Methods.* A total of 1858 subjects comprising 76% female, hypertensive, aged 18 and above were recruited into the study from two centers in Ibadan, Nigeria. Hypertension was identified using JNCVII definition and was further grouped into four subtypes: controlled hypertension (CH), isolated systolic hypertension (ISH), isolated diastolic hypertension (IDH), and systolic-diastolic hypertension (SDH). *Results.* Systolic-diastolic hypertension was the most prevalent. Whereas SDH (77.6% versus 73.5%) and IDH (4.9% versus 4.7%) were more prevalent among females, ISH (10.1% versus 6.2%) was higher among males ($P = 0.048$). Female subjects were more obese ($P < 0.0001$) and SDH was prevalent among the obese group. *Conclusion.* Gender and obesity significantly influenced the distribution of the hypertension subtypes. Characterization of hypertension by subtypes in genetic association studies could lead to identification of previously unknown genetic variants involved in the etiology of hypertension. Large-scale studies among various ethnic groups may be needed to confirm these observations.

1. Introduction

Cardiovascular disease is the world's number one killer. World Heart Federation statistics reveal that cardiovascular diseases account for 17.3 million deaths per year, and by 2030 this is expected to rise to 23 million. Hypertension remains a worldwide phenomenon being a major component of cardiovascular diseases with life-time cumulative incidence approaching 50% in many populations [1]. Mass migration from rural to peri-urban and urban areas with improved industrialization and adoption of western diets and lifestyle changes have led to steady increase in incidence of hypertension in Africa [2, 3]. In sub-Sahara alone, about 10–20 million people have hypertension with various degrees of target organ damages [4]. Based on the data available, the African Union has identified hypertension as one of its challenges after AIDS [3, 5].

In Nigeria, the prevalence of hypertension is on the increase among both the rural and urban settlers with resultant rising trends of sudden cardiac death [6–9]. Currently about 36 million Nigerians are estimated to have hypertension and its associated complications [9]. Despite all the advances in the study and management of hypertension, the control remains very poor. Salako et al. [10] found only 25.4% of subjects studied in a clinical setting had both systolic blood pressure (SBP) and diastolic blood pressure (DBP) controlled. Uncontrolled hypertension accounts for substantial proportion of cardiovascular deaths and morbidity resulting from stroke, heart failure, acute myocardial infarction, and kidney failure [11–13]

Prevention of hypertension and its control can markedly reduce cardiovascular morbidity and mortality; however the multifactorial aetiopathophysiologic mechanism of hypertension makes control difficult. A complex relationship

within the environment and genetics accounts for the etiology of this disease. While the environmental factors such as obesity, diet (especially high sodium, low potassium, and excess energy intake), stress, and physical inactivity are easily elucidated, the genetic determinants of hypertension remain obscure. Heterogeneity within patient subsets and attempts to combine all hypertensives together in the search of genes has made genetic study of hypertension highly challenging and mostly difficult. It is possible that hypertension is due to multiple distinct genes that can be studied better by subdividing hypertensive subtypes and this approach may help elucidate the genetics and pathophysiology of hypertension. The search for homogeneous hypertension subtypes has in the recent years widened the scope of our understanding of monogenic Mendelian hypertension [14]. It was shown that primary hypertension with hypokalemia has different pathophysiologic mechanism than those without hypokalemia. Also Jiménez et al. [15] described an association between predominantly diastolic hypertension (PDH) subtypes and the angiotensin-converting enzyme DD polymorphism in a small population of untreated patients with PDH. Most of the studies being undertaken to define the genetic influences have been in western societies where high levels of exposure to environmental risk factors prevail, especially obesity and excess sodium intake [16, 17]. To broaden the perspective on the subtypes of this condition we report a case series of subjects with hypertension at the University College Hospital and Adeoyo State Hospital Ibadan, Nigeria.

2. Materials and Methods

2.1. Study Design and Population. This cross-sectional descriptive study was conducted at the Medical Outpatient clinics of University College Hospital and Adeoyo State Hospital Ibadan, a secondary healthcare center, Oyo State, South West Nigeria. The two hospitals serve as referral centers for primary health care centers in Ibadan. Ibadan is the capital city of Oyo State in the south-western area of Nigeria and has a population of 3.6 million, while Oyo State has 5.6 million people according to the National Population census 2007. The Yoruba ethnic group is the major tribe in Ibadan city, while other major Nigerian ethnic groups like Igbo and Hausa are fairly represented. Christianity, Islam, and traditional religions are widely practiced in Ibadan. The city has a tropical wet and dry climate with a lengthy wet season and relatively constant temperatures throughout the course of the year. There are two peaks for rainfall, June and September. The mean maximum temperature is 26.46°C, minimum 21.42°C, and the relative humidity is 74.55%.

A total of 1858 hypertensive subjects, aged 18 years and above, of Yoruba tribe comprising 1411 females and 447 males were recruited into the study over two and half years between June 2009 and December 2011. Written informed consent was obtained from all participants. Only consenting participants of Yoruba tribe were included in the study. Subjects with fasting plasma glucose of greater than 126 mg/dL and plasma creatinine of greater than 1.5 mg/dL and those that refused consent were excluded from the study. The research protocol was approved by the joint Ethics Committee of the University College Hospital/University of Ibadan, Nigeria, and by the Institutional Review Board at Loyola University Medical Center, Maywood, IL, USA.

2.2. Data Collection. All measurements were conducted by one trained physician and two nurses between 8:00 am and 12:00 pm at Adeoyo State Hospital and 2 pm and 6 pm at medical outpatient, University College Hospital, Ibadan respectively. Blood pressure (BP) was measured using a standard Omron (HEM711DLX) blood pressure apparatus on the left arm after 5-minute rest using a cuff of appropriate size with the subject in the sitting position. Three BP measurements were obtained with a minimum interval of one minute and mean values were used in the analysis. Anthropometric measurements including height, weight, and waist and hip circumferences were obtained. Height was measured without shoes to the nearest centimeter using a ruler attached to the wall, while weight was measured to the nearest 0.1 kg on an electronic scale with the subject wearing light outdoor clothing and no shoes. Waist circumference was measured at the narrowest part of the participant's torso (or the minimum circumference between the rib cage and the iliac crest) [18] using an anthropometric measuring tape. The measurement was taken at the end of expiration. We measured waist circumference, recorded to the nearest tenth of a centimeter, 3 times and used the average of the 3 measurements.

Hypertension was defined as SBP ≥ 140 mmHg and/or DBP ≥ 90 mmHg or being on pharmacological treatment for hypertension. Hypertension subsubtypes were defined as follows: controlled hypertension (CH) if on antihypertensive medication, SBP < 140 and DBP < 90; isolated systolic hypertension (ISH) if SBP ≥ 140 and DBP < 90; isolated diastolic hypertension if SBP < 140 and DBP ≥ 90; systodiastolic hypertension (SDH) if SBP ≥ 140 and DBP ≥ 90; and predominantly diastolic hypertension (PDH) group as subjects having a pulse pressure (PP) to DBP ratio < 0.45.

Obesity was classified based on body mass index (BMI) in kg/m^2 as normal (<25 and >20), overweight (>25 and <30), obesity (>30 and <35), and severe obesity (≥35). Abdominal obesity was defined as waist circumference of greater than or equal to 102 cm in men and greater than or equal to 88 cm in women.

2.3. Statistical Analysis. Data was analyzed using the Statistical Package for Social Sciences (SPSS Inc, Chicago, IL) version 15. Results were expressed as either mean values (±standard deviation) or proportions. Comparison for statistical significance was by independent Student's t-test for continuous variables or chi-square for categorical variables. One way analysis of variance (ANOVA) with Bonferroni's post hoc method was used to compare the demographic and BP indices among the various BP subtype groups. The level of significance was set at $P \leq 0.05$.

3. Results

A total of 1858 hypertensive subjects (mean age 49 ± 9years) comprising 1411 females and 443 male participants were

Table 1: Basic characteristics of the population.

Variable	Female (n = 1411)	Male (n = 447)	Total (n = 1858)	P value
Age (yrs)	48.9 (8.29)	47.2 (10.58)	48.5 (8.92)	<0.002*
Weight (kg)	70.7 (15.20)	71.2 (14.15)	70.9 (15.66)	0.521
Height (m)	1.6 (0.07)	1.7 (0.07)	1.61 (8.09)	<0.001*
Arm circumference (cm)	29.1 (4.14)	27.8 (3.12)	28.8 (4.01)	<0.001*
Heart rate	89.7 (16.42)	85.9 (15.85)	89.1 (18.61)	<0.001*
Systolic blood pressure (mmHg)	161.6 (25.50)	161.2 (24.15)	161.8 (26.99)	0.766
Diastolic blood pressure (mmHg)	101.4 (14.07)	100.6 (15.23)	101.4 (15.80)	0.338
Body mass index (kg/m^2)	28.1 (5.80)	25.2 (4.80)	29.13 (7.27)	<0.001*
BMI groups				<0.001*
Normal	376 (28.5)	199 (49.8)	575 (33.4)	
Overweight	447 (33.9)	140 (35.0)	587 (34.1)	
Obese	320 (24.2)	52 (13.0)	372 (21.6)	
Severe obesity	177 (13.4)	9 (2.3)	186 (10.8)	
Waist-to-height ratio	0.708 (0.16)	0.712 (0.14)	0.709 (8.10)	0.635
Abdominal obesity	496 (35.1)	42 (9.4)	969 (51.6)	<0.001*

*Statistically significant.

recruited into the study. The characteristics of the study population classified by gender are as shown in Table 1. Females were significantly older, shorter, and heavier and had greater arm circumference and increased heart rates when compared with males. Blood pressure parameters were comparable among females and males. Anthropometric measurements showed that 587 (34.1%) were overweight, 372 (21.6%) obese, and 186 (10.8%) severely obese. Compared with males, female subjects were significantly more obese ($P < 0.0001$). Similarly 51.6% of the study population had abdominal obesity with female preponderance ($P < 0.0001$). Also as seen in Figure 1, there was significant effect of obesity on the distribution of hypertension subtypes. As shown in Figure 2, SDH (77.6% versus 73.5%) and IDH (4.9% versus 4.7%) are more prevalent among females compared with males, whereas the prevalence of ISH (10.1% versus 6.2%) and CH (11.7% versus 11.3%) was higher among males. Table 2 showed age group and gender relations of hypertension subsubtypes. While there was significant gender effect on the frequency of blood pressure subgroup, the age group did not affect the blood pressure subtypes. The frequency of the different hypertension subtypes among the 1858 hypertensive subjects was as follows: controlled hypertension 11.4%, isolated diastolic hypertension (IDH) 4.8%, isolated systolic hypertension (ISH) 7.2%, and systolic and diastolic hypertension (SDH) 76.6%. Predominantly diastolic hypertension (PDH) was observed in 329 (17.7%) of the entire study population, 56 (26.4%) of CH, 72 (80%) of IDH, and 201 (14.1%) of SDH. We observed significant differences between hypertension subtype groups in essentially all the physiologic and anthropometric parameters (Table 3). SDH (77.6% versus 73.5%) and IDH (4.9% versus 4.7%) are more prevalent among females compared with males, whereas the prevalence of ISH (10.1% versus 6.2%) and CH (11.7% versus 11.3%) was higher among males.

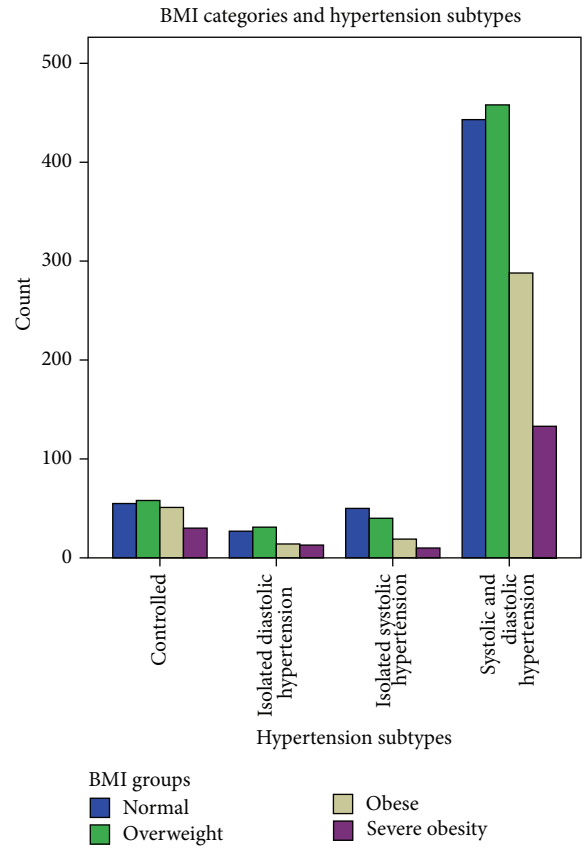

Figure 1: BMI categories and hypertension subtypes.

4. Discussion

This study shows that hypertension is a phenotype consisting of heterogeneous subtypes. The pooling of hypertension

Table 2: Age group and gender relations of hypertension subtypes.

	Controlled hypertension ($n = 212$)	Isolated diastolic hypertension ($n = 90$)	Isolated systolic hypertension ($n = 133$)	Systolic and diastolic hypertension ($n = 1423$)	P value
Gender					<0.048
Females	160 (11.3)	69 (4.9)	88 (6.2)	1096 (77.6)	
Males	52 (11.7)	21 (4.7)	45 (10.1)	327 (73.5)	
Age group					0.254
Young (≤39 yrs)	14 (6.6)	11 (12.2)	13 (9.8)	107 (7.5)	
Middle age (40–59 yrs)	185 (87.3)	76 (84.4)	107 (80.5)	1201 (84.4)	
Elderly (≥60 yrs)	13 (6.1)	3 (3.3)	13 (9.8)	115 (8.1)	

Table 3: Comparisons of demographic and BP indices in the hypertension subtypes.

Parameters (means)	Controlled	Isolated diastolic hypertension	Isolated systolic hypertension	Systolic and diastolic hypertension	P value
Age	48.80 (8.52)[a]	45.40 (8.78)[b]	50.14 (9.56)[a]	48.51 (8.88)[a]	<0.001*
SBP	122.98 (11.46)[a]	133.15 (5.80)[b]	155.33 (12.56)[c]	169.98 (28.83)[d]	<0.001*
DBP	80.14 (6.64)[a]	97.18 (9.47)[b]	84.58 (4.90)[c]	106.41 (13.85)[d]	<0.001*
Waist	95.02 (13.53)[c]	93.41 (12.23)[b,c]	90.08 (11.84)[a]	90.78 (12.48)[a,b]	<0.001*
Pulse	83.47 (15.22)[a]	92.40 (16.09)[c]	87.70 (25.11)[a]	89.83 (18.36)[b,c]	<0.001*
Waist-to-height ratio	0.74 (0.16)[b]	0.72 (0.17)[a,b]	0.69 (0.15)[a]	0.71 (0.16)[a]	<0.003*
BMI	28.14 (6.23)[b]	27.89 (5.98)[b]	25.97 (5.39)[a]	27.46 (6.24)[b]	<0.014*
PDH ratio**	0.54 (0.15)[a]	0.38 (0.10)[b]	0.84 (0.18)[c]	0.60 (0.19)[d]	<0.001*
Weight	74.35 (15.94)[b]	72.06 (16.85)[a,b]	68.63 (14.63)[a]	70.56 (15.57)[a]	<0.003*
Height	162.85 (7.41)[b]	160.56 (9.63)[a]	162.63 (8.02)[b]	160.50 (8.03)[a]	<0.001*

[a,b,c,d]Means with the same superscript are not different at $P < 0.05$.
*Statistically significant.
**PDH ratio = pulse pressure/diastolic pressure.

patients without consideration for the heterogeneous nature of hypertension subtype in genetic association mapping for hypertension may have contributed to the limited success in identification of genetic variants involved in the etiology of hypertension to date.

Interestingly, studies have shown that the frequencies of various hypertension subtypes depend on the age of the cohorts studied. While some found IDH to be more prevalent among young adults others found it more prevalent among the elderly [19–23]. In the present study, subjects with IDH accounted for 4.8% of the total population and were significantly younger than those of the other groups. A report from China contradicts an early claim that linked IDH blood pressure profile with low cardiovascular risk [24]. It was demonstrated in that study that although less than ISH and SDH, patients with IDH had higher rates of cardiovascular diseases than normotensive individuals [19, 25]. Current findings of prevalent IDH among young cohort as shown in this study require increased research interest in this group of people to prevent further hypertension associated morbidity and mortality.

Isolated systolic hypertension (ISH) is a common "pulse pressure phenotype" that has been associated with increased cardiovascular risk. In Framingham's study [26], ISH was more common among the elderly. It was shown that, among the young adults, ISH was more likely to evolve from high normal or normal blood pressure but in the elderly it most likely emanates from systo-diastolic hypertension (SDH) and IDH making two distinct types of isolated systolic hypertension. These discrepancies might suggest different genetic influence for each type of ISH. Similarly in this study, ISH was more prevalent among the older subjects and also more prevalent than IDH, but the specific categories of ISH subtypes were not studied

The gender bias in favour of females in this particular study may be explained by the nature of the community where health seeking is considered as a feminine behavior until an illness becomes severe. In this study there was a clear evidence of gender influence on the risk factors associated with hypertension. Women were significantly older, shorter, and heavier and had greater arm circumference and heart rates when compared with men. This is similar to study by Ejim et al. [8] who found hypertensive women in the Eastern Nigeria community to be heavier, taller, and older than their male counterparts. Elevated heart rate has been shown to be a risk factor for cardiovascular morbidity and mortality especially among the hypertensive [27]. Other studies also showed that elevated heart rate potentiates the risk of metabolic disturbances, diabetes, and atherosclerosis and coronary artery diseases [28]. Significantly higher heart rates among

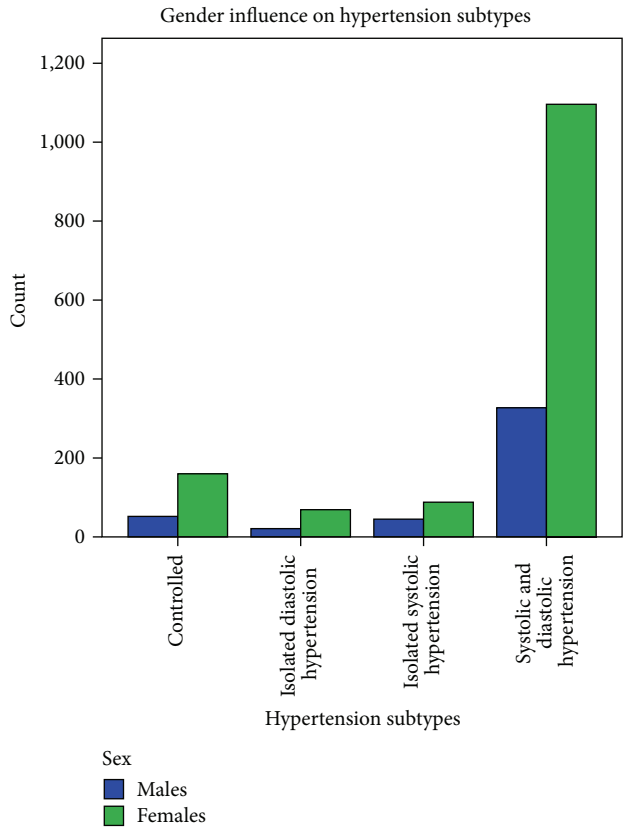

Figure 2: Gender influence on hypertension subtypes.

female as demonstrated in this study might potentiate the increased cardiovascular risk in them.

Some studies showed that patients with IDH have high prevalence of metabolic syndrome or increased body mass index [29, 30]. In our study the IDH subtypes had increased body mass index compared to the finding of Jiménez et al. [15]. From the foregoing, the IDH subsets in our study require more attention in terms of management of hypertension and prevention of cardiovascular morbidity and mortality.

Orias et al. [31] suggested that predominantly diastolic hypertension (PDH) describing SDH subsets with narrow pulse pressure tends to have similar hemodynamic patterns and are more homogenous. Also Jiménez and colleagues [15] described a link between PDH and angiotensin converting enzyme (ACE) polymorphisms in a small number of untreated hypertensives. Similar observation was reported in the Framingham cohort, which showed strong association between ACE genotype and diastolic blood pressure among men [26]. Using Blank and associates [20] definition, the prevalence of PDH in this study was 17.7% of general population accounting for 26.4% among CH, 80% of IDH, and 14.1% of SDH. PDH and IDH have been shown to have similar physiology which if it applies cumulatively makes the prevalence of IDH in this study almost 20% of the subject population. Some studies demonstrated the prevalence of IDH to be as high as 23%. When patients with PDH are added to the group, IDH may account for 30%–40% of subjects with essential hypertension [29]. Although not conclusive it is tempting to suggest from the study that 20–25% of our studypopulation have similar haemodynamic and genetic makeup. This may suggest an association between this group and ACE genotype.

This study has shown that the heterogeneity of hypertension may also determine the degree of blood pressure control among subjects with hypertension. Gender and obesity significantly influenced the distribution of the hypertension subtypes. Prevention or control of hypertension would be better if the various subtypes are well understood. From this study, reasons for the low frequency of controlled hypertension might just not be due to nonavailability of drugs or patients' poor drug adherence but also likely resulting from the varying prevalence and characteristic of hypertension subtypes as elucidated in this work.

Our study has the following limitations. The findings of this study's results may not be generalizable to the whole population because individuals attending hospital may have other comorbidities that were not taken into cognizance in this study. There is the possibility of sessional variation bias in population survey of blood pressure. However, Ibadan city has a tropical wet and dry climate with a lengthy wet season and relatively constant temperatures throughout the course of the year; we tend to believe that seasonal variation could not have significantly affected our findings in this study. Also, since the subjects were hypertensives on drug therapy, these could have introduced some misclassification into the subtype determination.

5. Conclusion

We have characterized the heterogeneous nature of hypertension with the predominantly Yoruba-speaking population of southwest Nigeria. As part of effort to identify genetic variants involved in the etiology of hypertension, the different hypertension subtypes may warrant individual consideration. Future research endeavors might focus on the young adults with isolated diastolic hypertension to prevent potential early cardiovascular morbidity and mortality. Larger studies in multiple populations may be needed to provide further insight into this.

Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

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