Prevalence and predictors of resistant hypertension among out-patients in Ilorin, Nigeria

James Ayodele Ogunmodede[1] and Olalekan Ayodele Agede[2]

1. Department of Medicine, University of Ilorin, Kwara state, Nigeria
2. Department of Pharmacology, University of Ilorin, Kwara state, Nigeria

Correspondence:
James Ayodele Ogunmodede
Email: ayodeleogunmodede@yahoo.com

Submitted: November 2022
Accepted: February 2023
Published: May 2023

Citation: Ogunmodede and Agede, Prevalence and predictors of resistant hypertension among out-patients in Ilorin, Nigeria, South Sudan Medical Journal, 2023;16(2):50-54 DOI: https://dx.doi.org/10.4314/ssmj.v16i2.3

ABSTRACT

Introduction: Systemic hypertension (SH) contributes the highest number of deaths from cardiovascular diseases worldwide. Patients with resistant hypertension (RH) are more prone to hypertension-mediated organ damage. RH has not been well-studied in Africa, despite the fact that the prevalence of SH is highest in Africa. The aim of the study was to establish the prevalence and predictors of RH among out-patients managed in the cardiology unit of the University of Ilorin Teaching Hospital, Ilorin, Nigeria.

Method: A cross-sectional study of 201 patients selected via systematic random sampling between April and September 2019.

Results: Mean age of the participants was 59.6 (SD 13.8) years, females 58.7%, 32.3% were non-obese, 17 (8.5%) consumed alcohol and three (1.5%) smoked tobacco. 30 participants (14.9%) had co-morbid diabetes mellitus. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were significantly higher among patients with RH 152.5 (SD 18) mmHg vs 131.9 (SD 18.4) mmHg (p<0.001) and 89.43 (SD 13.8) mmHg vs 79.46 (SD 10.5) mmHg (p=0.008). Eighteen patients (8.96%, 95% CI: 5.5-14%) had RH. The predictors of RH were obesity (OR= 3.754; p=0.009), SBP at patients' first clinic visit, (OR=1.029, p=0.032), DBP at patients' first clinic visit, (OR=1.048, p=0.014), and serum phosphorus, (OR=1.047, p=0.047).

Conclusion: The prevalence of RH among our patients is low and is similar to that in studies with similar blood pressure cut-off values and case definition.

Keywords: resistant hypertension; predictors; obesity; serum phosphorus; systolic blood pressure; diastolic blood pressure

INTRODUCTION

Systemic hypertension (SH) accounts for the highest number of deaths from cardiovascular diseases worldwide. With a prevalence of about 30% among hypertensives,[1] Africa bears a considerable burden of hypertension compared to elsewhere. Awareness, treatment, and control are low.[2,3] Despite the availability of a broader range of antihypertensive medications and increasing awareness of the dangers of hypertension, control is achieved in only about 50%[4] and as low as 33% in some places outside Africa.[5]

Resistant hypertension (RH) refers to uncontrolled blood pressure (BP) despite the concurrent use of three antihypertensive drugs, including a diuretic, prescribed at optimally tolerated dosages with the exclusion of pseudo-hypertension, white coat hypertension and non-adherence to medications. It also includes patients whose blood pressures are controlled but with four or more antihypertensive medications, including a diuretic prescribed at an optimally tolerated dosage.[6,7,8]

African studies on RH are few. Even fewer studies are capturing the burden of RH in the African setting.[9,10] Despite being the region with the highest burden

of SH, the prevalence of RH may also, in like fashion, be very high.

The objectives of this study were to establish the prevalence of RH among patients managed in the outpatient medical clinics of our hospital and identify factors associated with the development of RH.

METHOD

This cross-sectional study was conducted in the cardiology clinic of University of Ilorin Teaching Hospital (UITH) Ilorin, north-central Nigeria. We defined the study population as the estimated 6 monthly attendance of hypertensives at the clinic (406) and used Yamane's formula[11] to determine the sample size (201). We therefore sampled every second patient aged 18 years or more.

Informed consent was obtained from eligible patients and ethical approval from the Department of Medicine. The research was done according to the principles of the Helsinki declaration.[12]

Data was collected between June 1 and November 30, 2019. Adherence to treatment was assessed using 8-item Morisky Medication Adherence Scale which had been used in a previous study.[13] The score was given on an ordinal scale: 8 indicating a high level of adherence, 6 to <8, medium and <6 low adherence. Participants were considered to have RH when they had medium or high levels of medication adherence in addition to standard criteria.[14]

The BP was measured three times using a mercury sphygmomanometer and an appropriately sized BP cuff. The first measurement was performed after participants had rested, seated for five minutes with a 60-second interval between readings. The average of the three measurements was calculated. Controlled BP was defined as SBP <140 mmHg and DBP <90 mmHg.[15] Obesity was defined as BMI values ≥ 30kg/m2, estimated glomerular filtration rate (eGRF) from the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula.[14]

Data was analysed using SPSS software version 22. Patients' characteristics were summarized into means or medians for continuous data and categorical variables as percentages. Chi-square tests and Student's independent t-tests were used to test for associations between categorical and normally distributed continuous variables respectively and the presence or otherwise of RH. Mann–Whitney U test was used to compare medians of skewed variables. A binary logistic regression was performed to ascertain the predictors of RH among the patients. The variables that showed a significant association with the presence of RH were inputted into the regression model. Statistical significance was set at $p < 0.05$.

RESULTS

The mean age of the participants was 59.6 (SD13.8) years. There were 118 (58.7%) females, 65 were obese (32.3%, p=0.006), 17 (8.5%) consumed alcohol and 3 (1.5%) smoked tobacco. Other socio-demographic parameters are in Table 1. Table 2 shows that the mean SBP, DBP,

Table 1. Socio-demographic variables of study participants

	All patients	Patients without RH	Patients with RH	
	Mean [SD]/ Median (IQR)/Frequency (%)	Mean [SD]/ Median (IQR)/Frequency (%)	Mean [SD]/ Median (IQR)/Frequency (%)	p-value
	201	183 (91.04)	18(8.96)	
Age	59.58 [13.77]	59.52 [13.8]	60.21 [13.9]	0.845
Gender: Male	83 (41.3)	72 (86.7)	11 (13.3)	
Female	118 (58.7)	111 (94.1)	7 (5.9)	0.074
Obese	65 (32.3)	54 (83.1)	11 (16.9)	
Alcohol intake	17 (8.5)	17 (100.0)	0 (0.0)	0.177
Smoking	3 (1.5)	3 (100.0)	0 (0.0)	0.584
Coexisting DM				
Yes	30 (14.9)	27 (90)	3 (10)	0.828
Family History of Hypertension				
Yes	92 (45.7)	81 (88.9)	11 (11.1)	0.383
Duration of Hypertension diagnosis (years)				
Yes	7 (2-15)	7 (2-13)	7 (2-15)	0.968

Table 2. Comparison of clinical and laboratory variables of participants with and without resistant hypertension

	All patients Mean [SD]	Patients without RH Mean [SD]	Patients with RH Mean [SD]	p-value
Current Systolic BP (mmHg)	133.7 [19.3]	131.9 [18.4]	152.5 [18]	**<0.001***
Current Diastolic BP (mmHg)	80.4 [11.1]	79.46 [10.5]	89.4 [13.8]	**0.008***
Systolic BP on first clinic visit (mmHg)	143.3 [18.8]	142.4 [18.5]	152.4 [19.6]	**0.030***
Diastolic BP on first clinic visit (mmHg)	87.3 [13.4]	86.5 [13.3]	94.8 [13.1]	**0.013***
Serum Sodium (mmol/l)	139.6 [18.7]	137.8 [4.6]	139.7 [3.3]	0.093
Serum Potassium (mmol/l)	3.6 [0.6]	3.6 [0.6]	3.5 [0.7]	0.549
Serum Urea (mmol/l)	4.4 [1.9]	4.4 [1.9]	4.9 [2.4]	0.459
Serum Creatinine (µmol/l)	88.7 [29.6]	88.7 [29.2]	92.6 [24.9]	0.652
eGFR (ml/min/1.73m2)	74.5 [24.4]	74.6 [24.6]	74.3 [27.1]	0.968
Serum Calcium (mmol/l)	2.4 [0.5]	2.3 [0.28]	2.6 [0.14]	**<0.001***
Serum Phosphate (mmol/l)	**1.6 [1.3]**	1.2 [0.46]	1.96 [0.4]	**0.012***
Serum TCHOL (mmol/l)	5.1 [1.3]	5.1 [1.40]	4.3 [1.1]	0.071
Serum HDL (mmol/l)	1.1 [0.4]	1.1 [0.42]	0.4 [0.4]	0.063
Serum LDL (mmol/l)	4.1 [5.2]	3.6 [1.3]	3.1 [1.1]	0.358
Serum Triglyceride (mmol/l)	1.47 [0.5]	1.21 [0.5]	1.37 [0.4]	0.374

eGFR- Estimated Glomerular Filtration Rate; TCHOL- Total cholesterol; HDL- High Density Lipoprotein; LDL- Low Density Lipoprotein.

serum calcium and phosphate were significantly higher among patients with RH p<0.001, p=0.008, p<0.001, p<0.001 and p=0.012 respectively. The prevalence of DM and family history of SH were similar in patients with and without RH.

The BP of 37 patients (18.5%) was controlled with four or more antihypertensive drugs or were on three drugs without achieving BP control. Among these, 11 (5.5%) were poorly adherent to medications, three (1.5%) were not on diuretics and five (2.5%) were not on maximum doses of antihypertensive drugs. Only 18 subjects (8.96%, 95% CI: 5.5-14%) had RH in this study.

The predictors of RH were obesity (OR=3.754; p =0.009), SBP at patients' first clinic visit, (OR=1.029, p=0.032), DBP at patients' first clinic visit, (OR=1.048, p= 0.014), and serum phosphorus (OR=2.414, p =0.047) (see Table 3).

DISCUSSION

The prevalence of RH of 8.96% in this study is at variance from the rest of Africa where rates range from 5–30%. [7,15] In a meta-analysis of studies of RH over a 28-year period, out of the 91 studies found, only five were done in Africa.[9,15]

The varying rates of RH arise from inconsistent methodology, sample size, BP cut-off values for RH, and consideration of adherence to medication.[10,16-17] In an Ibadan, Nigeria, study 5% had RH.[16] However, individuals with poor medication adherence (about half of the study participants) were not excluded from those adjudged to have RH. The finding of 7.3% in an Algerian study[17] is comparable with ours because patients with poor compliance were excluded. Compared to the rest of the world, the prevalence of RH in our study, though higher than the 5% reported in France[18], is less than the pooled data of 10.3% reported in the general population of 3.2 million hypertensives in a meta-analysis by Noubiap et al.[15]

The association between obesity and RH has been reported previously in Africa.[20] The renin-angiotensin-aldosterone pathway is enhanced in obese individuals[19] and there is a greater inhibition of the natriuretic peptide system, blunting beneficial vasodilatation and natriuresis.

This study found that the initial BP at first clinic visit was significantly higher in patients who had RH, a finding also reported by the Antihypertensive and Lipid-Lowering and Treatment to Prevent Heart Attack investigators.[20] This suggests that patient-related factors which predispose to treatment resistance may bestow patients with higher BP values from the onset of the disease. The finding that serum phosphate was significantly lower in the patients with RH agrees with that of Alonso et al[21] although the mechanism is obscure but differs from that of Patel et al.[22] Serum calcium is higher in our patients with RH. Higher serum total calcium levels were positively

Table 3. Predictors of resistant hypertension by binary logistic regression

		β	p-value	Odds ratio	95% CI	
					Lower	Upper
Obesity	Not Obese [Ref]	1.323	0.009*	3.754	1.382	10.20
	Obese					
Systolic BP at first clinic visit		0.028	0.032*	1.029	1.002	1.056
Diastolic BP at first clinic visit		0.047	0.014*	1.048	1.009	1.089
Serum Phosphorus		3.184	0.047*	2.414	1.047	556.5
Serum Calcium		4.812	0.175	123.027	0.118	127.5
eGFR		-0.001	0.965	0.999	0.973	1.026

eGFR- Estimated Glomerular Filtration Rate.

associated with hypertension in a large sample of United States adults. However, in our study, it was not predictive of RH probably due to our relatively small sample size.[23]

Our study is limited by sample size and non-usage of ambulatory BP monitoring (ABPM) facilities which are limited. Judd and Calhoun[7] have suggested that RH, identified in the absence of ABPM, might be misclassified as having RH.

CONCLUSION

Our study confirms a variation in prevalence of RH among African hypertensive patients and reports a prevalence similar to studies with the same BP cut-off values and case definition. Our study contributes to defining the burden of RH in the Africa and is important for designing strategies to achieve better BP control.

Conflicts of interest: None

Sources of funding: Self

Acknowledgement: Authors acknowledge Mr Medubi for his editorial assistance

References

1. World Health Organization. Global status report on non-communicable diseases 2014: "attaining the nine global noncommunicable diseases targets; a shared responsibility". Geneva: World Health Organization, 2014.
2. Dzudie A, Kengne AP, Muna WF, Ba H, Meninga A, Kouam CK. Prevalence, awareness, treatment and control of hypertension in a self-selected sub-Saharan African urban population: a cross-sectional study. BMJ Open 2012;2: pii:e001217
3. Lloyd-Sherlock P, Beard J, Minicuci N, Ebrahim S, Chatterji S. Hypertension among older adults in low- and middle-income countries: prevalence, awareness and control. Int J Epidemiol 2014;43:116–28.
4. Olanrewaju TO, Aderibigbe A, Chijioke A, Sanya EO, Busari OA, Kolo PM, et al. Descriptive analysis of blood pressure control among treated hypertensive patients in a tertiary hospital in Nigeria. Afr J Med Med Sci. 2011;40(3):207–212.
5. Chen G, Chen F, Sun K, Yuan TT, Zhang X. Prevalence and determinants of resistant hypertension among hypertensive patients attending a cardiology clinic in China: a prospective cross-sectional study. Tropical Journal of Pharmaceutical Research 2016; 15 (10): 2261-2267.
6. The Nigerian Hypertension Society. Guidelines for the management of hypertension in Nigeria 2020. Mosuro Publishers. p35.
7. Judd E, Calhoun DA. Apparent and true resistant hypertension: definition, prevalence and outcomes. Journal of Human Hypertension 2014;28(8):463-8
8. Daugherty SL, Powers JD, Magid DJ, Tavel HM, Masoudi FA, Margolis KL, et al. Incidence and prognosis of resistant hypertension in hypertensive patients. Circulation 2012; 125:1635–1642.
9. Nansseu JRN, Noubiap JJN, Mengnjo MK, Aminde LN, Essouma M, Jingi AM, et al. The highly neglected burden of resistant hypertension in Africa: a systematic review and meta-analysis. BMJ Open 2016;6:e011452.
10. Yaméogo NV, Samadoulougou AK, Kagambèga LJ, Millogo GRC, Yaméogo AA, Kologo KJ, et al. Epidemiological characteristics and clinical features of black African subject's resistant hypertension. Ann Cardiol Angiol (Paris) 2014;63:83–8.
11. Yamane T. Statistics, An Introductory Analysis, 2nd Ed., New York: Harper and Row. 1967 p61.

12. World Medical Association. World Medical Association declaration of Helsinki: ethical principles for medical research involving human subjects. JAMA 2013;310(20):2191-2194.

13. Akintunde AA, Akintunde TI. Antihypertensive Medications Adherence Among Nigerian Hypertensive Subjects in a Specialist Clinic Compared to a General Outpatient clinic. Annals of Medical and Health Sciences Research 2015;5:173-178

14. Levey AS, Stevens LA. Estimating GFR using the CKD Epidemiology Collaboration (CKD-EPI) creatinine equation: more accurate GFR estimates, lower CKD prevalence estimates, and better risk predictions. Am J Kidney Dis. 2010;55(4):622-627.

15. Noubiap JJ, Nansseu JR, Nyaga UF, Sime PS, Francis I, Bigna JJ. Global prevalence of resistant hypertension: a meta-analysis of data from 3.2 million patients. Heart. 2019 Jan 1;105(2):98-105.

16. Salako BL, Ayodele OE. Observed factors responsible for resistant hypertension in a teaching hospital setting. Afr J Med Med Sci 2003; 32:151–4.

17. Henine N, Kichou B, Kichou L, Benbouabdellah M, Boubchir MA, Madiou A, et al. Prevalence of true resistant hypertension among uncontrolled hypertensive patients referred to a tertiary health care center. Annales de Cardiologie et d'Angéiologie 2016; 65(3):191-196.

18. Rosenbaum D, Villeneuve F, Gury C, Girerd X. Frequency of hypertension resistant to treatment and indication for renal denervation. Ann Cardiol Angeiol (Paris). 2012;61(3):229–233. doi:10.1016/j.ancard.2012.04.018.

19. Engeli S, Sharma AM. The renin-angiotensin system and natriuretic peptides in obesity-associated hypertension. J Mol Med 2001;79:21-29.

20. Cushman WC, Ford CE, Cutler JA, Margolis KL, Davis BR, Grimm RH, et al for the ALLHAT Collaborative Research Group. Success and predictors of blood pressure control in diverse North American settings: the Antihypertensive and Lipid-Lowering and Treatment to Prevent Heart Attack Trial (ALLHAT). J Clin Hypertens. 2002; 4: 393–404.

21. Alonso A, Nettleton JA, Ix JH, de Boer IH, Folsom AR, Bidulescu A, et al. Dietary phosphorus, blood pressure and incidence of hypertension in the Atherosclerosis Risk in Communities (ARIC) Study and the Multi-Ethnic Study of Atherosclerosis (MESA) Hypertension. 2010 Mar; 55(3): 776–784.

22. Patel RK, Jeemon P, Stevens KK, Mccallum L, Hastie CE, Schneider A, et al. Association between serum phosphate and calcium, long -term blood pressure, and mortality in treated hypertensive adults. J Hypertens 2015;33(10):2046-2053.

23. Sabanayagam C, Shankar A. Serum Calcium Levels and Hypertension Among US Adults. The Journal of Clinical Hypertension 2011;13: 716-721