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Resistant hypertension: Prevalence and profile of patients followed in a university ambulatory

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Abstract

Background: Hypertension affects about 36 million Brazilians. It is estimated that 10%–20% of these have resistant hypertension. These patients are at an increased risk of early target organ damage, as well as cardiovascular and renal events.

Objective: To estimate the prevalence of resistant hypertension in a specialized outpatient clinic, to describe the sociodemographic and clinical characteristics of these patients, and to identify possible factors associated with resistant hypertension.

Methods: Data collection from medical records of hypertensive patients treated using oral antihypertensive drugs in optimized doses at a specialized university clinic from March 2014 to December 2014, after ethical approval statement. All patients were using appropriate antihypertensive drugs in optimized doses and assisted at a teaching-assistance clinic of internal medicine of the Bahiana School of Medicine and Public Health in Brazil.

Results: A total of 104 patients were enrolled and 31.7% (n = 33) had criteria for resistant hypertension. Of the total participants, 75.7% were female and 54.8% were black or brown. The average age was 61.7 years (SD ± 10.1). In the resistant hypertension group, 63.6% had diabetes, compared to 32.4% in the hypertension group. Among resistant hypertensive patients, 51.5% had dyslipidemia. Regarding drug treatment, 75.8% of the resistant hypertension group and 51.4% of the hypertension group used statins. Among patients with resistant hypertension, 90.9% used angiotensin II receptor blockers and 66.7%, dihydropyridine calcium channel blockers. In the resistant hypertension group, 75.8% used beta-blockers, against 25.4% in the hypertension group.

Conclusion: The prevalence of hypertension was higher than that described in the global literature, which may be associated with the high percentage of black and brown ("pardos") patients in the population studied, and also because the study was performed in a specialized outpatient clinic.

Keywords

Hypertension, prevalence, antihypertensive agents/therapeutical use, drug resistance

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Introduction

Hypertension is defined as systolic blood pressure (SBP) ⩾140 mmHg and/or diastolic blood pressure (DBP) ⩾90 mmHg.[1–3] The VIGITEL 2019 survey (Surveillance of Risk and Protection Factors for Chronic Diseases by Telephone Survey) from Brazil's Ministry of Health found that among adults 24.5% have self-reported hypertension, which affects 59.3% of adults aged 65 and over 55.5% of men and 61.6% of women.[4]

It is known that nationwide surveys by telephone interviews using self-reporting underestimate the actual prevalence of diseases. A systematic review with meta-analysis of Brazilian population studies[5] found a prevalence of 36.1%. Considering world BP control, almost less than half of hypertensive patients had adequate blood pressure control.[6–9]

Resistant hypertension (RH) is defined as elevated BP above the target in a hypertensive patient notwithstanding the use of optimized doses of three oral antihypertensive drug classes, usually including a long-acting diuretic, a selective calcium channel blocker, and a renin–angiotensin system blocker. RH also comprises patients whose BP achieves target control with ⩾4 antihypertensive medications.[10,11] Refractory hypertension is defined as a special subgroup of hypertensive patients who keep their BP uncontrolled (BP ⩾ 140/90 mmHg) even using five or more antihypertensive drug classes, including a properly diuretic, considering their fluid status and renal function, and for whom spironolactone has been added to the treatment plan.[10–12]

The diagnosis of true RH depends on the patient's compliance, changes in lifestyle, and drug treatment, as well as the exclusion of inappropriate BP measurement techniques. Equally, it is necessary to perform ambulatory blood pressure monitoring (ABPM) or home blood pressure monitoring (HBPM) to rule out the diagnosis of white coat hypertension (WCH) or masked hypertension (MH) as causes of false RH.[11,13,14]

Population studies estimate that 10%–20% of hypertensive patients have RH.[6,7,15] In Brazil, the multicentric ReHOT study found a prevalence of 11.7%.[16] This group of patients has no response to treatment, presents multifactorial etiology, and has a higher incidence of early target organ damage and cardiovascular (CV) and renal events when compared to controlled hypertensive patients.[8,12,17] Thus, this study aims to estimate the prevalence, to describe sociodemographic and clinical characteristics, as well as associated risk factors of RH patients in an outpatient specialized clinic, which is an important tool in a context of scarce data in a developing country such as Brazil.

Methods

Population selection and study period

A descriptive, analytical, cross-sectional observational study, with a convenience sample, of a systematic type, including data from adult hypertensive patients over 18 years of age with the prescription appropriate antihypertensive drugs in optimized doses, consecutively seen at the teaching-assistance clinic of internal medicine of the Bahiana School of Medicine and Public Health (EBMSP) and who had all predetermined variables documented. The period established was from 1 March 2014 to 15 December 2014. The exclusion criteria were patients under investigation of or diagnosed with secondary hypertension, patients with WCH or masked hypertension, and patients using medications that could justify poor BP control.

Analyzed variables

The following variables were studied: age, gender, ethnicity (self-reported skin color), marital status, education, family income, alcohol consumption, smoking, physical activity, number and classes of antihypertensive drugs used, documented preexisting diagnosis of diabetes mellitus (DM), dyslipidemia, stroke or acute myocardial infarction (AMI), preexisting clinical diagnosis of angina or heart failure, albuminuria, serum creatinine, changes in echocardiogram, statin use, waist circumference, and body mass index (BMI) with obesity diagnosis (those with BMI values above 30 kg/m^2).

Data collection protocol

Data from the initial visit were collected in person, relating to the complete anamnesis and physical examination of all patients, including office BP measurement, as recommended in the VI Brazilian Guidelines on Hypertension,[18] in three different moments after 5 min of rest, in the sitting position with automatic devices validated and calibrated with cuffs appropriate to the brachial circumference, with a minimum interval of 5 min between them, according to the center's protocol.

All participants were asked to perform routine complementary tests: serum creatinine, electrolytes, serum lipid, and glycemia data, urinalysis, and albuminuria. These variables were evaluated in a return visit, with an approximate interval of 90 days. Electrocardiogram results and serum uric acid levels were not included among the variables analyzed due to information gaps. Subsequently, the remaining complementary data, such as the echocardiogram results, which were not always available at the return visit, were obtained from the medical records.

For all patients, ABPM or HBPM were used to rule out pseudoresistance.[19] In cases where it was not possible to perform one of these two methods, patients were instructed to measure BP at a Basic Health Unit with trained professionals, always obtaining records in duplicate, in the morning before breakfast and at the end of the day before dinner, for seven consecutive days and before the medical visit.

Sample size calculation

The sample size was calculated using the formula: $N = Z^2 \times P \times Q/E^2$, with Z being the confidence level, P the estimated

prevalence, E the desired precision, and Q a constant (1P). With Z values of 1.96 (considering a 95% confidence interval), a prevalence of resistant hypertension of 10%, and a desired precision of 5%, the required sample would be 118 patients. Before the conclusion of the data collection, data were analyzed with n sample of 60 patients and the prevalence of RH was 10%.

Ethical considerations

The data collection project was submitted to the Ethics and Research Committee (ERC) of Santo Antônio Hospital, Salvador, Bahia, Brazil. The approval certificate from the ERC was received, and the registration number is 30504314.1.0000.0047.

Statistical analysis

For the build-up of the database and the necessary analysis, the SPSS® v.21.0 software for Windows was used.

Descriptive statistics was used to calculate measures of central tendency and dispersion of the quantitative variables studied, as well as the frequencies of categorical variables. Shapiro–Wilk and Kolmogorov–Smirnov tests were used to check the type of distribution of the variables studied. The Chi-square test was used to compare proportions and the Student's t-test was used to compare means for variables with a Gaussian distribution.

To perform multivariate logistic regression, the backward stepwise method was used. The selection of variables to be included in the regression was based on the following criteria: $p < 0.10$ when comparing the hypertension (HPTN) group and the RH group and biological plausibility.

The level of significance adopted in the statistical tests was 5% ($p < 0.05$).

Results

Initially, although 183 participants were selected, 47 were excluded due to lack of information on HBPM and 32 due to incomplete information about the classes of antihypertensive drugs used, resulting in a total of 104 individuals in the study, later divided into resistant hypertensive patients (RH group) and nonresistant hypertensive patients (HPTN group). Among them, 75.7% were female and the average age was 61.7 years (SD ± 10.1). Most individuals were black or brown, corresponding to 54.8% of the sample, and reported not practicing any physical activity (62.5%). Only 37 patients (35.6%) reported alcohol consumption and 25% reported smoking (Table 1).

The prevalence of RH found in this sample was 31.7% (33 patients), 84.8% were female, and 72.7% were black or brown. The average age was 62.2 years (SD ± 9.6). Only three patients (9.1%) in the RH group reported smoking and 36.4% reported consuming alcoholic beverages. Most patients were sedentary (66.7%). Table 2 describes the sociodemographic characteristics of the group with RH.

Table 1. Sociodemographic characteristics of the sample and resistant hypertension prevalence.

Variables	N (%)
Gender	
Female	78 (75.7)
Male	26 (24.3)
Schooling	
Illiterate	9 (7.9)
Incomplete primary school	51 (49.5)
Incomplete secondary school	17 (15.8)
Complete secondary school	27 (26.7)
Family income	
One salary	57 (54.5)
Two salaries	29 (28.7)
Three salaries	11 (9.9)
Four salaries	7 (6.9)
Marital status	
Married	49 (47.1)
Widowed	16 (15.7)
Single	28 (27.5)
Divorced	11 (9.8)
Ethnicity (black or brown skin)	
No	47 (45.2)
Yes	57 (54.8)
Smoking	
No	78 (75.0)
Yes	26 (25.0)
Consumption of alcoholic beverages	
No	67 (64.4)
Yes	37 (35.6)
Physical activity	
No	65 (62.5)
Yes	39 (37.5)
Resistant hypertension	
No	71 (68.3)
Yes	33 (31.7)

When the two groups were compared, the average SBP in the RH group was 145.7 mmHg (SD ± 27.4), against 142.7 mmHg (SD ± 27.1) in the HPTN group. The average DBP among patients with RH was 87.7 mmHg (SD ± 13.2) and 87.1 mmHg (SD ± 12.3) among patients with hypertension. The average abdominal circumference was 101.6 cm (SD ± 20.6) in the RH group and 98.2 cm (SD ± 27.4) in the HPTN group. The average BMI was 27.6 kg/m^2 (SD ± 3.0) and 26.6 kg/m^2 (SD ± 3.2) in the RH and HPTN groups, respectively. Average albuminuria in the sample with RH was 21.9 mg/g (SD ± 27) versus 15.9 mg/g (SD ± 13.7) in patients with RH ($p = 0.730$), and the average serum creatinine was 1.1 mg/dL (SD ± 0.2) in the RH group and 1.0 mg/dL (SD ± 0.2) in the HPTN group. Among these variables, only serum creatinine, despite the difference of only 0.1 mg/dL between the two groups, showed a statistically significant difference ($p = 0.019$). Table 3 describes the above-mentioned results.

Table 2. Comparison of sociodemographic characteristics between patients with hypertension and resistant hypertension.

Variables	HPTN Group N (%)	RH Group N (%)	*p**
Gender			0.106**
Female	51 (71.4)	28 (84.8)	
Male	20 (28.6)	5 (15.2)	
Schooling			0.385
Illiterate	4 (5.8)	4 (12.5)	
Incomplete primary school	37 (52.2)	14 (43.8)	
Incomplete secondary school	10 (13.0)	8 (21.9)	
Complete secondary school	20 (29.0)	7 (21.9)	
Family income			0.915
One salary	38 (53.5)	18 (56.7)	
Two salaries	20 (28.2)	9 (30.0)	
Three salaries	8 (11.3)	3 (6.7)	
Four salaries	5 (7.0)	3 (6.7)	
Marital status			0.801
Married	31 (43.5)	18 (54.5)	
Widowed	12 (17.4)	4 (12.1)	
Single	20 (29.0)	8 (24.2)	
Divorced	8 (10.1)	3 (9.1)	
Ethnicity (black or brown skin)			0.012
No	38 (53.5)	9 (27.3)	
Yes	33 (46.5)	24 (72.7)	
Smoking			0.008**
No	48 (67.6)	30 (90.9)	
Yes	23(32.4)	3 (9.1)	
Consumption of alcoholic beverages			0.909
No	46 (64.8)	21 (63.6)	
Yes	25 (35.2)	12 (36.4)	
Physical activity			0.550
No	43 (60.6)	22 (66.7)	
Yes	28 (39.4)	11 (33.3)	

HPTN: hypertension; RH: resistant hypertension.
*Chi-square test; **Fisher test; t: total of patients in each group.

Table 3. Comparison of clinical and laboratory data between patients with hypertension and resistant hypertension.

Variables	Mean ± SD*		*p***
	HPTN Group t = 71	RH Group t = 33	
Age (years)	61.5 ± 10.4	62.2 ± 9.6	0.929
LDL-c (mg/dL)	128.6 ± 28.8	127.3 ± 25.5	0.918
HDL-c (mg/dL)	60.9 ± 4.7	60.9 ± 3.7	0.875
Triglycerides (mg/dL)	148.7 ± 23.9	154.4 ± 36.3	0.328
Glycemia (mg/dL)	98.5 ± 27.3	101.9 ± 20.2	0.169
Abdominal circumference (cm)	98.2 ± 27.4	101.6 ± 20.6	0.196
BMI (kg/m^2)	26.6 ± 3.2	27.6 ± 3.0	0.126
SBP (mmHg)	145.7 ± 27.4	142.7 ± 21.1	0.947
DBP (mmHg)	87.7 ± 13.2	87.1 ± 12.3	0.874
Weight (kg)	73.2 ± 15.6	74.9 ± 16.3	0.843
Height (m)	1.6 ± 0.1	1.6 ± 0.1	0.871
Albuminuria (mg/g)	15.9 ± 13.7	21.9 ± 27.0	0.730
Creatinine level (mg/dL)	1.0 ± 0.2	1.1 ± 0.2	0.019
Time since diagnosis (years)	6.9 ± 2.2	6.4 ± 2.8	0.133
Number of antihypertensives	1.6 ± 0.5	3.4 ± 0.5	0.000

BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; t: total of patients in each group.
*Standard Deviation; **Student's t test.

Regarding clinical characteristics, 63.6% of the RH group had a diagnosis of DM, while only 32.4% of the HPTN group had this same comorbidity ($p = 0.003$). Dyslipidemia was diagnosed in 17 patients (51.5%) in the RH group ($p = 0.632$). The diagnosis of heart failure was found in 15.2% of the patients with RH, 6 (18.2%) reported past angina, and 3 (9.1%) previous AMI in this same group. Echocardiogram showed LVH in 12.1% of the RH group, against 9.9% in the HPTN group, while diastolic dysfunction was identified in 8.5% of the HPTN group and 18.2% of the RH group. Most patients in the RH group used statins (75.8%). In the HPTN group, this rate was only 25.4%.

As for the medication regimen, β-blockers were present in 75.8% of the cases of RH, while in the HPTN group only 25.4% used it ($p = 0.000$). Diuretics and angiotensin II receptor blockers (ARBs) were the most used classes in both groups—90.9% and 81.8% in the RH group and 42.3% and 46.5% in the HPTN group, respectively. Calcium channel blockers (CCBs) appeared in 66.7% of the therapeutic regimens of patients with RH and 26.8% of the HPTN group ($p = 0.000$). The average number of classes of antihypertensive drugs used by patients with RH was 3.4 (SD ± 0.5). The clinical data assessed in the two groups are summarized in Table 4.

For multivariate analysis, among the variables with biological plausibility, those with $p < 0.10$ were included, namely: skin color, DM, use of β-blockers, and use of CCB (Table 5).

Table 4. Comparison of clinical data between patients with hypertension and resistant hypertension.

Variable	HPTN Group, N (%) t = 71	RH Group, N (%) t = 33	p*
Dislipidemia			0.632
No	38 (53.5)	16 (48.5)	
Yes	33 (46.5)	17 (51.5)	
Diabetes			0.003
No	48 (67.6)	12 (36.4)	
Yes	23 (32.4)	21 (63.6)	
Angina			0.589
No	55 (77.1)	27 (81.8)	
Yes	16 (22.9)	6 (18.2)	
Acute myocardial infarction			0.432**
No	62 (87.3)	30 (90.9)	
Yes	9 (12.7)	3 (9.1)	
Stroke			0.497**
No	65 (91.4)	31 (93.9)	
Yes	6 (8.6)	2 (6.1)	
Heart failure			0.240**
No	65 (91.5)	28 (84.8)	
Yes	6 (8.5)	5 (15.2)	
Echocardiogram			0.490
Normal	52 (73.2)	21 (63.6)	
LVH	7 (9.9)	4 (12.1)	
Signals of ischemia	6 (8.5)	2 (6.1)	
Diastolic dysfunction	6 (8.5)	6 (18.2)	
Use of statin			0.019
No	34 (48.6)	8 (24.2)	
Yes	37 (51.4)	25 (75.8)	
Up to 2 antihypertensives			0.000**
No	4 (5.6)	33 (100.0)	
Yes	67 (94.4)	0 (0.0)	
Therapeutic regimen including β-blocker			0.000
No	53 (74.6)	8 (24.2)	
Yes	18 (25.4)	25 (75.8)	
Therapeutic regimen including diuretic			0.000**
No	41 (57.7)	3 (9.1)	
Yes	30 (42.3)	30 (90.9)	
Therapeutic regimen including CCB			0.000
No	52 (73.2)	11 (33.3)	
Yes	19 (26.8)	22 (66.7)	
Therapeutic regimen including ACE inhibitors			0.395
No	57 (80.3)	28 (84.8)	
Yes	14 (19.7)	5 (15.2)	
Therapeutic regimen including ARB			0.001
No	38 (53.5)	6 (18.2)	
Yes	33 (46.5)	27 (81.8)	

ACE: angiotensin-converting enzyme; ARB: angiotensin receptor blocker; CCB: calcium channel blocker; t: total of patients in each group.
*Chi-square test; **Fisher test.

Discussion

The estimated prevalence of RH in the world varies between 10% and 20% of the hypertensive population.[6,7,17] The main Brazilian study about this subject found a similar prevalence in Brazil, about 11.7% of hypertensive patients.[16] In our study, the RH prevalence found was 31.7%. The higher rate might be explained by the fact that it concerns a specialized outpatient clinic for hypertensive patients dependent on the Brazilian public healthcare system (SUS) with low income and education levels[20] and also due to the ethnic composition of the population in Bahia. According to Brazilian Institute of Geography and Statistics data, more than 78% of the population from Bahia is composed of brown or black individuals.[21] This racial composition can result in a higher prevalence of hypertension and, consequently, of RH, which can be confirmed by the percentage of almost two-thirds of black and brown patients in the RH group. There was a statistically significant difference to the HPTN group, in which only 46.5% were Afro descendants. This data suggest an association of ethnicity with RH, which is widely corroborated by several studies that included black race as one of the risk factors for hypertension.[2,9,22,23] No research about RH prevalence in Bahia was found until the submission of this study. Another reason for the high prevalence of RH is the fact that we cannot exclude pseudo resistance. Therefore, it is possible that some of the patients included in this article, even met the inclusion criteria, have only apparent RH and some patients have true RH.

Table 5. Logistic regression for resistant hypertension.

	Odds Ratio	*p*	CI (95%)
Ethnicity (brown or black skin)	3.35	0.039	1.06–10.46
Diabetes	4.28	0.010	1.41–12.97
β-blocker use	10.69	0.000	3.34–34.17
CCB use	4.05	0.013	1.36–12.30

CCB: calcium channel blocker; CI: confidence interval.

Another factor known to be associated with hypertension is age, which is one of the causes for the increased global prevalence of hypertension since life expectancy around the world has increased significantly in recent decades. In Brazil, since 1940, 30.8 more years have been added to life expectancy.[24] The average age of the sample was over 60 years, in line with national and global data, in which the prevalence of hypertension can reach 60% when considering only the elderly population.[4,25] This finding is in accordance with an epidemiological study regarding hypertension in American adults that found similar results, demonstrating that age is an independent factor.[26]

The American Heart Association (AHA) and Centers for Disease Control and Prevention (CDC) consider the practice of physical activity as a protective factor against cardiovascular diseases, including hypertension, because it contributes to weight control and decrease in LDL-c levels.[27] Confirming these recommendations, in the sample evaluated, 60.6% of hypertensive patients and 66.7% of patients with RH stated that they did not practice any type of physical activity. A sedentary lifestyle is included in national and international hypertension guidelines as a risk factor for the development and worsening of hypertension.[2,3,28] A research carried out with patients with RH in the Brazilian state of Minas Gerais found an even higher proportion (77%).[29] Other national studies have also revealed that more than 50% of hypertensive individuals do not practice physical exercises[30–32] and, although measurement was not performed using specific tools for sedentary behavior, our findings are in accordance with the literature.[33]

The average SBP and DBP values found in both groups were similar. Although it is not possible to infer conclusions from the analysis of these two variables in isolation, this data may suggest selection bias, since the sample had a predominance of female elderly people who were in specialized outpatient follow-up, with established diagnosis and treatment. Such characteristics may be associated with a higher rate of therapeutic adherence, which may have reflected a better pressure control in both groups,[34] despite adherence not being measured by objective instruments, but questioned in detail in all medical visits.

In regard to clinical aspects, the higher prevalence of DM ($p = 0.003$) and dyslipidemia in patients with RH in relation to patients with hypertension suggests a higher cardiovascular risk (CVR) related to RH.[35,36] Furthermore, the use of statins was more common among patients with RH, which may also be related to the elevated CVR and renal dysfunction risk in this group.[37] Although greater in the RH group, the difference between the prevalence of dyslipidemia in the two groups was lower than the difference found between the percentage of statin use. We must consider that the prescription of this medication is not exclusively dependent on serum cholesterol levels, being mainly associated with the assessment of the patient's CVR and considering the existence of a contraindication to its use.[37]

The prevalence of heart failure was higher in the RH group when compared with the HPTN group. Similarly, echocardiographic changes, such as LVH and diastolic dysfunction, were more frequent among patients with hypertension. From the renal standpoint, albuminuria and average serum creatinine were higher among patients with RH when compared to the levels found among patients with hypertension. Although only serum creatinine reached statistical significance ($p = 0.019$), all these data are compatible with those presented in the literature as RH is associated with a higher risk of early target organ injuries.[38–40]

In both groups, most patients did not show a significant change in echocardiogram (73.2% in the HPTN group and 63.6% in the RH group). Compared to the literature,[40,41] in the sample evaluated, the prevalence of echocardiographic changes was lower than expected, especially if we consider the average time of diagnosis of hypertension found in the sample of 104 patients: 6.7 years (SD ± 2.4). This finding might be explained by the use of medications that can reverse Left Ventricular Hyperthrophy (LVH), such as Renin Angiotensin Aldosterone System (RAAS) blockers.[42]

Still from a cardiological point of view, there was a significant rate of patients who reported the diagnosis of angina (21.4% in patients with hypertension and 18.2% in patients with RH, $p = 0.589$). An Italian study analyzed the occurrence of cardiovascular events for about 5 years in 340 hypertensive patients, 130 of whom had RH. The results of this study suggested a 2.94 times greater risk of cardiovascular events in patients with true RH when compared to patients with hypertension.[40]

The average number of antihypertensive drug classes used by patients with hypertension was 3.4, which is consistent with the literature, although we do not have fixed-dose combinations in the Brazilian public healthcare system, which could improve adherence.[43] As recommended by the hypertension and RH treatment guidelines,[10–12] ARB and diuretics were the most present classes in the therapeutic regimen of patients in this sample. High usage rates of these medications were already expected and confirmed, since their roles in controlling BP and some associated comorbidities and early target organ damage are already well defined. On the other hand, the proportion of patients with RH using β-blockers was higher than the number of CCB prescriptions, considered the third drug to be included in the therapeutic regimen of these patients.[1–3,27,28,44]

Although it could be considered a contributing factor in the choice of β-blockers, the prevalence of heart failure and other heart diseases assessed in the sample would not justify the high percentage of this therapeutic class. It is possible that β-blockers were the fourth drug of choice at the time the data were collected since its use was considerably higher among patients with RH.

The percentage of use of each prescribed diuretic type was not detailed in the database, though it was possible to identify that none of the patients included in the study used spironolactone, a finding that might be different if the collection period had occurred in the last few years. Thus, it is worth mentioning that data collection was carried out in 2014, the year in which the 8th JOINT was published, and the Brazilian Guidelines for Hypertension in effect suggested β-blockers as being effective drugs in reducing BP, morbidity, and mortality in these patients.[29] From this time on, relevant clinical trials began to be published showing the efficacy of spironolactone in the control of RH and starting to suggest it as the fourth drug in an antihypertensive regimen.[16,45] Only after the 7th Brazilian Hypertension Guidelines,[2] released in 2016, did the Brazilian Societies of Cardiology, Nephrology, and Hypertension begin to consider β-blockers as fifth or sixth choice classes.

In the sample studied, there was a clear preference for choosing ARB rather than angiotensin-converting enzyme (ACE) inhibitors. A possible reason for this choice is an easier dosage of the ARB covered by the Brazilian public healthcare system, losartan, when compared to ACE inhibitor, captopril.

In the multivariate analysis, a possible association between the use of β-blockers, the use of CCB, DM, and ethnicity with RH was suggested. Several studies have suggested race as a risk factor for RH, especially if it is associated with other factors such as age.[3,15] Likewise, studies commonly suggest a higher prevalence of hypertension among diabetic patients.[2,4,9,10] An American study carried out between 1999 and 2004 evaluated BP control among 14,653 hypertensive patients and suggested that the percentage of controlled hypertension is lower when the patient also has DM.[46]

The association of certain drugs with RH has not been widely studied. Although most guidelines for hypertension treatment agree with the choice of the antihypertensive regimen, some medications still do not show well-established benefits in this context.[47]

Cardioselective β-blockers and those with vasodilatory properties have clear advantages in cardiac patients. However, when the aim is to control BP, these drugs face some issues. The main protocols for hypertension and RH suggest the use of β-blockers as the fifth or sixth class to be introduced, except in specific situations. On the other hand, CCBs are medications with a strong recommendation for inclusion in antihypertensive regimens, being suggested as a choice for the third drug.[1,2,9,10]

For the most part, the results of this study are in accordance with the data reported in the world literature. However, no similar study in Bahia was found in the period when the literature review was performed. Knowledge of the patient's sociodemographic and clinical profile allows for the targeted follow-up to their main demands, thereby facilitating the customization of multidisciplinary care as well as the choice of therapy.

Although the analyzed sample was restricted to a single outpatient center in Salvador, both the significant number of patients included in this study and the consonance of the results with those reported in the literature allow us to suggest that they can be generalized to populations with similar sociodemographic characteristics.

The limitations of this study are as follows. This study has a predominance of elderly female participants with self-reported brown or black skin color, which may give rise to selection bias. Objective instruments to measure adherence to treatment and sedentary behavior were not used, although for sedentary lifestyle the majority claimed never enrolling in any type of physical activity. Biochemical detection of medications in urine or blood samples are not routinely done in the Brazilian Public Health System (SUS), and we always considered physicians' perception and ask patients to report on their own medication adherence, bringing their pills and telling us how they take them, but we know that leads to inaccurate estimates. Because of the impossibility to exclude pseudo-RH (apparent resistant hypertension) by an objective method, we could not assume that we involved just patients with true RH, therefore possibly including some patients with apparent RH.

In addition, all patients included in this study were treated by SUS and the great majority of them were low-income patients. Because SUS does not cover all tests and patients cannot pay for them, it was exceedingly difficult to request expensive examinations, as renin and aldosterone level, for all of them. Finally, this study did not foresee the need to differentiate the type of diuretic chosen for antihypertensive treatment or the use of alternative medications, such as alpha-blockers and direct vasodilators, though this did not affect the analysis of the main therapeutic classes used.

Cohort studies are useful to identify which factors associated with RH have a causal link, but robust clinical trials such as the Brazilian study ReHOT[16] would be important to further support the evidence related to the choice of the fourth and fifth drugs in an antihypertensive regimen.

Conclusion

The prevalence of RH was higher than the estimated in the literature, which may be associated with the fact that the state of Bahia has a mostly black and brown population as well as the fact that older participants were included, predominantly sedentary, overweight and diabetic, all factors largely associated with RH. A high number of therapeutic classes for BP control was observed, including the preferential use of diuretics and ARB, in addition to β-blockers in patients with RH, even surpassing CCB, but the reasons for this choice

could not be established. Further studies are needed to better understand this more severe hypertension phenotype, which gives its patients a poor prognosis due to the high CV and renal dysfunction risks.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical approval

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Informed consent

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Supplemental material

Supplemental material for this article is available online.

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