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Original Article

Clinical Characteristics of Patients with Resistant Hypertension: A Cross-Sectional Analysis

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Abstract-

Background: Resistant hypertension (RHTN) is a clinically important phenotype associated with disproportionately high cardiovascular and renal risk. Although several scientific statements describe its predictors at a population level, single-centre data describing the clinical profile of confirmed RHTN remain valuable for guiding local screening and referral practice. ***Objective***: To describe the demographic, anthropometric, biochemical, and pharmacological characteristics of patients with true resistant hypertension attending a tertiary hypertension clinic, and to identify the secondary and contributory conditions most frequently associated with this phenotype. ***Methods***: In this cross-sectional, single-centre study, 180 adult patients fulfilling the American Heart Association/European Society of Hypertension criteria for resistant hypertension (office blood pressure ≥130/80 mmHg despite ≥3 optimally dosed antihypertensive agents including a diuretic, or controlled blood pressure on ≥4 agents) were enrolled after exclusion of white-coat effect by ambulatory blood pressure monitoring and confirmation of adherence. Demographic data, anthropometrics, laboratory parameters, target-organ damage, and prescribed antihypertensive regimens were recorded and analysed descriptively and by group comparison. ***Results***: The mean age was 58.6 ± 10.4 years, with a female predominance (54.4%) and a mean body mass index of 29.8 ± 4.6 kg/m². Chronic kidney disease (38.9%), obesity (44.4%), type 2 diabetes mellitus (35.6%), and obstructive sleep apnoea (31.1%) were the most prevalent associated conditions. A secondary cause of hypertension was identified in 26.1% of patients, most commonly primary aldosteronism (12.8%) and renal artery stenosis (5.6%). Left ventricular hypertrophy was present in 41.1% of patients. The mean number of antihypertensive agents was 3.8 ± 0.7, and a mineralocorticoid receptor antagonist had been added in only 33.9% of patients despite current guideline recommendations. ***Conclusion***: Patients with confirmed resistant hypertension in this cohort were characterised by a high burden of obesity, chronic kidney disease, diabetes, and obstructive sleep apnoea, with primary aldosteronism representing the leading identifiable secondary cause. Underuse of mineralocorticoid receptor antagonists suggests a gap between guideline recommendations and current prescribing practice that merits targeted clinical attention.

Keywords: *resistant hypertension; clinical characteristics; primary aldosteronism; obstructive sleep apnoea; chronic kidney disease; antihypertensive therapy.*

INTRODUCTION

Hypertension remains the leading modifiable risk factor for cardiovascular morbidity and mortality worldwide, and a substantial proportion of treated patients fail to achieve recommended blood pressure targets despite multidrug therapy (1,2). Resistant hypertension (RHTN) is defined by current American Heart Association and European Society of Cardiology/European Society of Hypertension statements as office blood pressure that remains above goal despite the concurrent use of three or more antihypertensive agents of different classes at optimal or maximally tolerated doses, one of which should ideally be a diuretic, or blood pressure that is controlled but requires four or more agents (2,3). Both statements emphasise that the diagnosis of *true* RHTN requires the exclusion of pseudo-resistance, which encompasses poor medication adherence, white-coat effect on office measurement, inadequate dosing, and improper blood pressure measurement technique; this distinction is most reliably made through ambulatory or home blood pressure monitoring (3,4).

Estimates of prevalence vary considerably according to the definition applied and the population studied. Population-based analyses using the stricter 2017 American College of Cardiology/American Heart Association blood pressure thresholds suggest that apparent treatment-resistant hypertension affects approximately 9–20% of treated hypertensive adults, while

large meta-analytic data spanning more than three million patients estimate the prevalence of confirmed, true RHTN at approximately 10% once pseudo-resistance has been excluded (4,5). This prevalence rises substantially in specific clinical subgroups, reaching nearly 23% among patients with chronic kidney disease and over 50% among renal transplant recipients (5). The clinical importance of RHTN extends well beyond its prevalence: patients with this phenotype carry a markedly higher risk of stroke, myocardial infarction, heart failure, progression of chronic kidney disease, and all-cause mortality compared with hypertensive patients whose blood pressure is controlled on fewer agents (2,6).

A substantial body of literature has characterised the demographic and clinical correlates of RHTN. Data derived from the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT) identified older age, higher baseline systolic blood pressure, left ventricular hypertrophy, obesity, diabetes mellitus, and impaired renal function as independent predictors of treatment resistance, with chronic kidney disease emerging as the strongest single predictor (6). Subsequent cohort studies have consistently reproduced this pattern, additionally implicating excessive dietary sodium intake, obstructive sleep apnoea, metabolic syndrome, and depression as important contributory and frequently overlapping factors (1,7). In the RESIST-POL study of patients with confirmed RHTN, obstructive sleep apnoea of at least moderate severity was demonstrated in nearly half of all participants, and a secondary cause of hypertension—most often primary aldosteronism—was identified in approximately one-quarter of patients (1). More recent single-centre data have similarly shown that patients with resistant hypertension carry a disproportionate burden of high or very high cardiovascular risk and a higher prevalence of chronic kidney disease, obesity, dyslipidaemia, smoking, and diabetes compared with patients whose hypertension is well controlled on standard regimens (8).

Despite this accumulating evidence, important gaps in management persist. Guidelines recommend the addition of a mineralocorticoid receptor antagonist, most commonly spironolactone, as the preferred fourth-line agent on the basis of randomised trial data demonstrating superior blood-pressure-lowering efficacy compared with alternative add-on therapies (3,9). Nevertheless, real-world prescribing data indicate that mineralocorticoid receptor antagonists remain considerably underused in clinical practice, and that screening for secondary causes—particularly primary aldosteronism, which may be substantially more prevalent in RHTN than previously recognised—is frequently incomplete (9,10). Demographic clustering, including older age, male sex, and Black race, has also been described as characteristic of the apparent-RHTN phenotype in large administrative datasets, underscoring the heterogeneity of this population across different healthcare settings (10).

Given the substantial cardiovascular and renal consequences of RHTN, alongside persistent evidence of under-recognition of secondary causes and under-treatment with guideline-recommended fourth-line therapy, there remains a clear clinical need for contemporary, setting-specific descriptions of the patient population affected by this condition. Such data can help clinicians anticipate the comorbidity burden likely to be encountered in patients referred for resistant hypertension and can inform local diagnostic and therapeutic pathways. The present study was therefore designed to characterise the demographic, anthropometric, biochemical, and pharmacological profile of patients with confirmed true resistant hypertension attending a tertiary hypertension clinic, and to determine the frequency of secondary and contributory causes within this population.

MATERIALS AND METHODS

Study Design and Setting

This was a cross-sectional, observational, single-centre study conducted in the hypertension and cardiology outpatient clinics of [Institution Name] over a defined enrolment period of 18 months. The study was approved by the Institutional Ethics Committee, and written informed consent was obtained from all participants prior to enrolment, in accordance with the principles of the Declaration of Helsinki (11).

Study Population

Consecutive adult patients (≥18 years) with a clinical diagnosis of hypertension who were referred for evaluation of inadequate blood pressure control despite multidrug therapy were screened for eligibility. Resistant hypertension was defined according to the 2018 American Heart Association Scientific Statement as office blood pressure ≥130/80 mmHg despite concurrent treatment with three or more antihypertensive agents from different pharmacological classes at maximally tolerated doses, including a diuretic where not contraindicated, or as blood pressure controlled to target while requiring four or more agents (3). To exclude pseudo-resistance, all candidates underwent 24-hour ambulatory blood pressure monitoring; patients with a mean ambulatory daytime blood pressure below 135/85 mmHg (consistent with white-coat effect) were excluded. Medication adherence was assessed through structured pharmacy refill review and pill counts at the screening visit, and patients with confirmed non-adherence were excluded. Patients with secondary hypertension already established as the sole driver of blood pressure elevation prior to enrolment, pregnancy, and end-stage renal disease requiring dialysis were also excluded.

Data Collection
Standardised data collection forms were used to record demographic information (age, sex, ethnicity), anthropometric measurements (weight, height, body mass index, waist circumference), duration of hypertension, smoking and alcohol history, and family history of hypertension or premature cardiovascular disease. Office blood pressure was measured in triplicate after five minutes of seated rest using a validated automated oscillometric device, with the mean of the second and third readings recorded, in accordance with current measurement guidelines (2). Laboratory investigations performed in all patients included serum creatinine with estimated glomerular filtration rate (CKD-EPI equation), fasting plasma glucose and glycated haemoglobin, fasting lipid profile, serum electrolytes, plasma aldosterone-to-renin ratio, and urinary albumin-to-creatinine ratio. Patients with a positive aldosterone-to-renin ratio screen underwent confirmatory testing in accordance with the Endocrine Society guideline for primary aldosteronism (12). Screening for obstructive sleep apnoea was performed using the Berlin Questionnaire followed by overnight polysomnography or home sleep apnoea testing in patients screening positive or with a high clinical suspicion. Renal artery duplex ultrasonography, with computed tomography or magnetic resonance angiography where indicated, was used to evaluate for renal artery stenosis. Echocardiography was performed to assess left ventricular mass index and to define left ventricular hypertrophy using standard sex-specific cut-offs.

Statistical Analysis
Continuous variables were tested for normality using the Shapiro–Wilk test and are presented as mean ± standard deviation or median (interquartile range) as appropriate; categorical variables are presented as frequencies and percentages. Comparisons between subgroups were performed using the independent-samples t-test or Mann–Whitney U test for continuous variables, and the chi-square or Fisher exact test for categorical variables, as appropriate. A two-sided p-value <0.05 was considered statistically significant. All analyses were performed using standard statistical software.

RESULTS
A total of 224 patients with apparent treatment resistance were screened, of whom 44 (19.6%) were excluded after ambulatory blood pressure monitoring confirmed white-coat effect or after non-adherence was identified, leaving 180 patients with confirmed true resistant hypertension included in the final analysis. The demographic and anthropometric characteristics of the study population are summarised in Table 1.

Table 1. *Baseline demographic and anthropometric characteristics of patients with resistant hypertension (n = 180)*

Characteristic	Value	Range / SD
Age, years (mean ± SD)	58.6	± 10.4
Sex, female, n (%)	98	(54.4%)
Sex, male, n (%)	82	(45.6%)
Body mass index, kg/m² (mean ± SD)	29.8	± 4.6
Waist circumference, cm (mean ± SD)	101.2	± 11.7
Duration of hypertension, years (median, IQR)	11	(6–18)
Current smoker, n (%)	41	(22.8%)
Family history of hypertension, n (%)	112	(62.2%)
Office systolic BP, mmHg (mean ± SD)	152.3	± 14.1
Office diastolic BP, mmHg (mean ± SD)	91.7	± 9.8

BP = blood pressure; IQR = interquartile range; SD = standard deviation.

The associated comorbidities and secondary causes identified in the cohort are shown in Table 2. Chronic kidney disease and obesity were the most prevalent associated conditions, while a secondary cause of hypertension was confirmed in just over one-quarter of patients, most frequently primary aldosteronism.

Table 2. *Associated comorbidities and secondary causes of hypertension among patients with resistant hypertension (n = 180)*

Condition	n	%
Obesity (BMI ≥ 30 kg/m²)	80	44.4%
Chronic kidney disease (eGFR < 60 mL/min/1.73m²)	70	38.9%
Type 2 diabetes mellitus	64	35.6%
Obstructive sleep apnoea (moderate–severe)	56	31.1%
Dyslipidaemia	61	33.9%
Metabolic syndrome	98	54.4%
Left ventricular hypertrophy	74	41.1%
Any secondary cause identified	47	26.1%
— Primary aldosteronism	23	12.8%
— Renal artery stenosis	10	5.6%
— Obstructive sleep apnoea as primary driver*	9	5.0%
— Other (thyroid dysfunction, drug-induced)	5	2.8%

*BMI = body mass index; eGFR = estimated glomerular filtration rate (CKD-EPI). *Classified as a secondary driver only where apnoea-hypopnoea index was severe (≥30/h) and judged the dominant contributing mechanism by the managing clinician.*

Pharmacological treatment patterns are detailed in Table 3. The mean number of antihypertensive agents prescribed was 3.8 ± 0.7. Renin-angiotensin system blockers, calcium channel blockers, and thiazide-type or thiazide-like diuretics formed the backbone of therapy in the majority of patients, while mineralocorticoid receptor antagonists, the guideline-preferred fourth-line agent, had been added in only just over one-third of patients.

Table 3. *Antihypertensive medication classes prescribed among patients with resistant hypertension (n = 180)*

Medication class	n	%
ACE inhibitor or ARB	168	93.3%
Calcium channel blocker	159	88.3%
Thiazide / thiazide-like diuretic	147	81.7%
Beta-blocker	78	43.3%
Mineralocorticoid receptor antagonist	61	33.9%
Loop diuretic	34	18.9%
Alpha-1 blocker	22	12.2%
Centrally acting agent	14	7.8%
Direct vasodilator	8	4.4%

ACE = angiotensin-converting enzyme; ARB = angiotensin II receptor blocker. Percentages do not sum to 100 as most patients received multiple classes concurrently (mean 3.8 ± 0.7 agents per patient).

When patients with an identified secondary cause were compared with those without, the secondary-cause group was significantly younger (mean age 52.1 vs 60.8 years, $p < 0.001$), had a higher mean office systolic blood pressure (158.4 vs 149.9 mmHg, $p = 0.01$), and were more likely to have hypokalaemia at baseline (29.8% vs 4.5%, $p < 0.001$), consistent with the high proportion of primary aldosteronism within this subgroup. No statistically significant difference in sex

distribution was observed between groups (p = 0.42). Patients with chronic kidney disease had a significantly higher mean number of antihypertensive agents (4.1 ± 0.6) compared with those with preserved renal function (3.6 ± 0.7, p < 0.001).

DISCUSSION

This study describes the demographic, clinical, and pharmacological profile of patients with confirmed true resistant hypertension attending a tertiary referral clinic, after rigorous exclusion of pseudo-resistance by ambulatory blood pressure monitoring and adherence assessment. Nearly one in five patients initially considered apparently resistant were reclassified after this evaluation, a proportion closely consistent with prior reports that approximately one-third of apparent resistance can be attributed to white-coat effect or non-adherence, underscoring the importance of out-of-office blood pressure confirmation before labelling a patient as truly resistant (4,13).

The comorbidity profile observed in this cohort closely mirrors that described in the foundational literature on resistant hypertension. Obesity and chronic kidney disease were the most prevalent associated conditions, consistent with ALLHAT-derived data identifying renal impairment as the single strongest predictor of treatment resistance, and with subsequent single-centre series in which chronic kidney disease and obesity were independently and strongly associated with the resistant phenotype (6,8). The high prevalence of metabolic syndrome and moderate-to-severe obstructive sleep apnoea observed here, at just over half and nearly one-third of patients respectively, parallels findings from the RESIST-POL cohort, in which sleep apnoea and metabolic syndrome were the most frequent associated conditions and frequently coexisted in the same patient (1). These overlapping phenotypes likely share common pathophysiological pathways, including sympathetic nervous system overactivity, sodium retention, and aldosterone excess, which together sustain treatment-resistant blood pressure elevation (7,14).

The frequency of confirmed secondary hypertension in this cohort, at just over one-quarter of patients, is consistent with previously reported rates of 24% in confirmed RHTN populations and supports current recommendations that systematic secondary-cause screening be performed in all patients meeting criteria for true resistance rather than reserved for those with atypical features alone (1,3). Primary aldosteronism was, as in prior series, the leading identifiable secondary cause; this finding aligns with a growing body of evidence suggesting that primary aldosteronism is substantially more common among patients with resistant hypertension than has traditionally been assumed, and that biochemical screening with the aldosterone-to-renin ratio is both feasible and clinically rewarding in this population (9,12). The clinical and biochemical profile distinguishing patients with a secondary cause in our cohort—younger age, higher systolic blood pressure, and a markedly higher prevalence of hypokalaemia—mirrors the classic presentation of mineralocorticoid excess and reinforces the value of targeted screening in patients presenting with these features.

A particularly notable finding was the underuse of mineralocorticoid receptor antagonists, prescribed in only one-third of patients despite robust randomised trial evidence, most notably from the PATHWAY-2 study, demonstrating that spironolactone produces superior blood-pressure-lowering efficacy compared with alternative fourth-line agents such as doxazosin or bisoprolol in patients with confirmed resistant hypertension (9). This gap between guideline recommendation and observed prescribing practice has been similarly described in large administrative cohorts of patients with apparent resistant hypertension, in which add-on therapy frequently favoured beta-blockers or centrally acting agents over mineralocorticoid receptor antagonists (10). Possible explanations include clinician concern regarding hyperkalaemia, particularly in patients with chronic kidney disease who constituted a substantial proportion of this cohort, as well as variable awareness of the comparative efficacy data supporting spironolactone as the preferred fourth-line agent. Given that chronic kidney disease was highly prevalent in our population, careful potassium and renal function monitoring would be required to safely expand mineralocorticoid receptor antagonist use, but the magnitude of underuse observed suggests that caution alone does not fully account for the gap and that broader efforts to align practice with guideline recommendations are warranted.

This study has several limitations. As a single-centre, cross-sectional study, the findings may not be generalisable to other populations or healthcare settings, and referral bias toward a tertiary hypertension clinic may have enriched the cohort for more complex or treatment-refractory cases. The cross-sectional design precludes causal inference regarding the relationships observed between comorbidities and treatment resistance. Although adherence was assessed through pharmacy refill review and pill counts, more objective methods such as directly observed therapy or therapeutic drug monitoring may have identified additional cases of covert non-adherence. Finally, the relatively modest sample size limited the statistical power available for multivariable analysis of independent predictors of secondary hypertension within this cohort. Despite these limitations, the consistency of our findings with previously published, larger, and methodologically rigorous cohorts strengthens confidence in their clinical relevance.

CONCLUSION

Patients with confirmed resistant hypertension in this cohort were characterised by a substantial burden of obesity, chronic kidney disease, type 2 diabetes mellitus, and obstructive sleep apnoea, frequently overlapping within the same individual. A secondary cause was identified in approximately one-quarter of patients, with primary aldosteronism predominating, reinforcing the importance of systematic biochemical screening in this population. The comparatively low rate of mineralocorticoid receptor antagonist use, despite strong evidence supporting its efficacy as the preferred fourth-line agent, highlights a persistent and clinically important gap between guideline recommendations and everyday prescribing practice. These findings support a structured diagnostic approach to resistant hypertension—incorporating confirmation by ambulatory blood pressure monitoring, adherence assessment, and routine secondary-cause screening—alongside renewed clinical attention to guideline-concordant use of mineralocorticoid receptor antagonists, in order to improve blood pressure control and reduce the excess cardiovascular and renal risk associated with this condition.

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